

Supporting Information For:

A Diversity-Oriented, Split-Pool Synthesis of Biaryl-Containing Medium Rings.

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Experimental Techniques and Apparatus

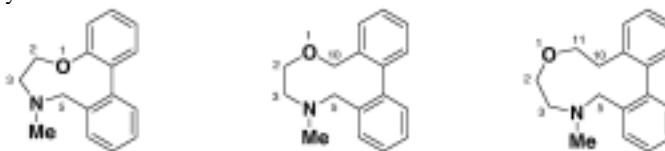
Except as otherwise indicated, reactions were carried out under argon with dry, freshly distilled solvents. Anhydrous 2-methyltetrahydrofuran (Aldrich, racemic) was stored over activated molecular sieves. Dry solvents were dispensed from a delivery system which passes the solvents through packed columns (tetrahydrofuran, diethyl ether, acetonitrile, and methylene chloride: dry neutral alumina; hexane, benzene, and toluene: dry neutral alumina and Q5 reactant; dimethylformamide: activated molecular sieves). *n*-BuLi in hexane (Aldrich), *s*-BuLi (Aldrich) in cyclohexane, *t*-BuLi in pentane (Aldrich), MeLi in diethyl ether (Aldrich) and *i*-PrMgCl in diethyl ether (Aldrich) were titrated with 1,10-phenanthroline and anhydrous 2-butanol before use.¹ All other reagents were purified in accordance with the instructions in "Purification of Laboratory Chemicals"² or used as obtained from commercial sources.

Yields refer to chromatographically and spectroscopically pure compounds. All reactions were monitored by thin layer chromatography (TLC) using glass plates precoated with Merck silica gel 60 F₂₅₄ or aluminum oxide 60 F₂₅₄. Visualization was by the quenching of UV fluorescence ($\lambda_{\text{max}} = 254$ nm) or by staining with ceric ammonium molybdate or potassium permanganate or Dragendorff's reagent (0.08% w/v bismuth subnitrate and 2% w/v KI in 3M aq. AcOH). Retention factors (*R_f*) are quoted to 0.01. Melting points were obtained using a Mel-Temp II melting point apparatus and are uncorrected. Infrared spectra were recorded either as a thin film between NaCl plates or as a KBr disc on a Nicolet 5PC FT-IR spectrometer with internal referencing. Absorption maxima (ν_{max}) are reported in wavenumbers (cm⁻¹) and the following abbreviations are used: w, weak; m, medium; s, strong; br, broad. Proton magnetic resonance spectra were recorded on Varian Mercury400 (400MHz), Bruker Avance DMX500 (500MHz), and Varian Unity/Inova500 (500MHz) spectrometers.³ Proton assignments are supported by ¹H-¹H COSY, HMQC, NOESY and GOESY spectra where necessary. Chemical shifts (δ_{H}) are quoted in ppm and are referenced to tetramethylsilane (internal). Coupling constants (*J*) are reported in Hertz to the nearest 0.5Hz. Data are reported as follows: chemical shift, integration, multiplicity [br, broad; s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; sept, septet; m, multiplet; or as a combination of these (e.g. dd, dt, etc.)], coupling constant(s) and assignment. Diastereotopic protons are assigned as X and X', where the ' indicates the lower field proton. Carbon magnetic resonance spectra were recorded on Varian Mercury400 (100MHz) and Varian Unity/Inova500 (125MHz) spectrometers. Carbon spectra assignments are supported by DEPT editing and where necessary ¹³C-¹H (HMQC) correlations. Chemical shifts (δ_{C}) are quoted in ppm to the nearest 0.01 ppm, and are referenced to tetramethylsilane (internal). Fluorine magnetic resonance spectra (¹⁹F) were recorded on a Varian Mercury300 (282MHz) spectrometer. Chemical shifts (δ_{F}) are quoted in ppm to the nearest 0.01 ppm and are referenced to

CF₃CH₂OH (external).⁴ Low resolution mass spectra⁵ were obtained with JEOL AX-505H, SX-102A (CI/EI), Micromass Platform II and LCT (APCI/ES/LCMS) spectrometers. Only molecular ions, fractions from molecular ions and other major peaks are reported. High resolution mass spectra was obtained with a Micromass LCT (ES) spectrometer, and reported mass values are within the error limits of ± 5 ppm mass units.⁶ Microanalyses were performed by E&R Microanalytical Laboratory, Inc. (Parsippany, NJ) and Robertson Microlit Laboratories, Inc. (Madison, NJ),⁷ and are quoted to the nearest 0.1% for all elements except for hydrogen, which is quoted to the nearest 0.05%. Reported atomic percentages are within the error limits of $\pm 0.4\%$.

X-ray Data:⁸ X-ray crystallographic data were collected by Dr. Richard J. Staples (Harvard University)⁹ using a Bruker SMART CCD (charge coupled device) based diffractometer¹⁰ equipped with an LT-2 low-temperature apparatus operating at 213K. A suitable crystal was chosen and mounted on a glass fiber using grease. Data were measured using omega scans of 0.3° per frame for 30 seconds, such that a hemisphere was collected. A total of 1271 frames were collected with a maximum resolution of 0.75Å. The first 50 frames were recollected at the end of data collection to monitor for decay. Cell parameters were retrieved using SMART¹¹ software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software¹² which corrects for Lp and decay. Absorption corrections were applied using SADABS¹³ supplied by George Sheldrick. The structures were solved by the direct method using the SHELXS-90¹⁴ program and refined by least squares method on F², SHELXL-97,¹⁵ incorporated in SHELXTL-PC V 5.10.¹⁶ All non-hydrogen atoms were refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. All drawings were done at 50% ellipsoids.

NMR Assignments: For clarity, the following numbering system has been used consistently for the biaryl ring systems:



General Experimental Procedures (Solution-Phase):

Reductive Alkylation of Amines.

(1) Mono-alkylation of Primary Amines. A round-bottomed flask, equipped with a magnetic stirring bar, containing the primary amino alcohol (1.0 equiv.) and benzaldehyde (1.0 equiv.; e.g. 2-iodobenzaldehyde¹⁷) was charged with MeOH (1M).

(4) Ribeiro, A.; Glen, M. J. *J. Magn. Reson., Ser. A* **1994**, *107*, 158-166.

(5) See: http://paula.harvard.edu:80/mass/facility_web_page.htm

(6) By Dr. Andrew Tyler, Jennifer A. Lynch and Qing Liao.

(7) See: <http://www.robertson-microlit.com/>

(8) Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (deposit@ccdc.cam.ac.uk). For detailed structural analysis of the biaryl medium rings, including crystal data and Chem3D files, see: http://www-schreiber.chem.harvard.edu/home/research_results.html

(9) See: <http://xriris2.harvard.edu/>

(10) The CCD based x-ray diffractometer at Harvard University was purchased through NIH grant (1S10RR11937-01).

(11) SMART V 5.050 (NT) Software for the CCD Detector System; Bruker Analytical X-ray Systems, Madison, WI (1998).

(12) SAINT V 5.01 (NT) Software for the CCD Detector System Bruker Analytical X-ray Systems, Madison, WI (1998).

(13) SADABS. Program for absorption corrections using Siemens CCD based on the method of Robert Blessing; Blessing, R.H. Acta Cryst. A51 (1995) 33-38.

(14) Sheldrick, G. M. SHELXS-90, Program for the Solution of Crystal Structure, University of Göttingen, Germany, 1990.

(15) Sheldrick, G. M. SHELXL-97, Program for the Refinement of Crystal Structure, University of Göttingen, Germany, 1997.

(16) SHELXTL 5.10 (PC-Version), Program library for Structure Solution and Molecular Graphics; Bruker Analytical X-ray Systems, Madison, WI (1998).

(17) 2-Iodobenzaldehyde was synthesized following the published procedure: Wissniewski, Grissom, J.; Klingberg, D.; Huang, D.; Slattery, B. J. *J. Org. Chem.* **1997**, *62*, 603-626. **2-Iodobenzaldehyde**. White solid; yield: 92%; m.p. 35-36°C (lit. 38-39°C; Gibson, S. E.; Guillo, N.; Middleton, R. J.; Thuilliez, A.; Tozer, M. J. *J. Chem. Soc., Perkin Trans. I* **1997**, 447-455); *R_f* 0.62 (SiO₂; Hexane: EtOAc; 4:1);

(1) Watson, S. C.; Eastham, J. F. *J. Organometal. Chem.* **1967**, *9*, 165-168.

(2) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals, Fourth Edition*; Butterworth-Heinemann: Oxford, 1997.

(3) See: <http://nmrhc.harvard.edu:80/nmr/lab/>

The solution was stirred at room temperature for 1-12 hours (TLC, oxazolidine formation), cooled to 0°C and then NaBH₄ (2.0 equiv.) was added in portions over 30 minutes [Caution! Hydrogen gas evolved]. The mixture was stirred allowing the reaction temperature to slowly rise to room temperature over 1-12 hours. An aqueous solution of NaOH (2M) and EtOAc was added and the resulting two-phase mixture was separated and then the aqueous phase was extracted two times with EtOAc. The combined organic layers were washed (saturated aqueous NaCl), dried (K₂CO₃), filtered, concentrated *in vacuo* and chromatographed.

(S)-2-(2-Iodobenzylamino)-3-phenyl-propan-1-ol; 1a. White solid; yield: 88%; m.p. 90-92°C; R_f 0.40 (SiO₂; Hexane: EtOAc; 1:1); δ_H (500MHz, CDCl₃) 2.30 (2H, br s, OH & NH), 2.76-2.86 (2H, m, PhCH₂), 2.94-2.99 (1H, m, NCH), 3.39 (1H, dd, J11, 5Hz, CHH'OH), 3.70 (1H, dd, J11, 4Hz, CHH'OH), 3.80 (2H, s, NCH₂Ar), 6.95 (1H, td, J7.5, 2Hz, aryl CH), 7.16-7.30 (7H, m, aryl CH), 7.79 (1H, dd, J8, 1Hz, aryl CH); δ_C (125MHz, CDCl₃) 38.10, 55.46, 59.29, 62.45, 99.77, 126.43, 128.30, 128.57, 128.94, 129.16, 129.71, 138.24, 139.51, 141.73; *m/z* (ES) 368 (MH⁺, 100%). Found: C, 52.2; H, 4.95; I, 34.3; N, 3.7%. C₁₆H₁₈INO requires C, 52.3; H, 4.95; I, 34.6; N, 3.8%.

(S)-2-(2-Bromobenzylamino)-3-phenyl-propan-1-ol; 1a (Br). White solid; yield: 93%; m.p. 72-74°C; R_f 0.33 (SiO₂; Hexane: EtOAc; 1:1); δ_H (500MHz, CDCl₃) 2.79-3.02 (3H, m, PhCH₂ and NCH), 3.42 (1H, dd, J11, 5Hz, CHH'OH), 3.71 (1H, dd, J11, 4Hz, CHH'OH), 3.90 (2H, s, NCH₂Ar), 7.11-7.33 (8H, m, aryl CH), 7.52 (1H, dd, J8, 1Hz, aryl CH); δ_C (125MHz, CDCl₃) 38.02, 51.05, 59.35, 62.37, 124.15, 126.45, 127.47, 128.56, 128.83, 129.14, 130.37, 132.87, 138.19, 138.52; *m/z* (ES) 320 (MH⁺, ⁷⁹Br, 100%), 322 (MH⁺, ⁸¹Br, 90%). Found: C, 60.0; H, 5.90; Br, 24.6; N, 4.3%. C₁₆H₁₈BrNO requires C, 60.0; H, 5.65; Br, 25.0; N, 4.4%.

(S)-2-(2-Bromo-4,5-dimethoxybenzylamino)-3-phenyl-propan-1-ol; 1. Colorless oil; yield: 87%; R_f 0.09 (SiO₂; Hexane: EtOAc; 1:1); ν_{max} (thin film)/cm⁻¹ 3279s, 3057m, 3023m, 2920s, 2840s, 1602m, 1510s, 1438s, 1377s, 1344s, 1255s, 1235s, 1210s, 1163s, 1066s, 1029s, 860s, 806s, 746s, 697s, 535s; δ_H (500MHz, CDCl₃) 1.49 (1H, br s, OH or NH), 2.72-2.82 (2H, m, PhCH₂), 2.91 (1H, br s, OH or NH), 3.03-3.06 (1H, m, NCH), 3.38 (1H, dd, J10.5, 5Hz, CHH'OH), 3.66 (1H, br d, J10.5Hz, CHH'OH), 3.75 (2H, br d, J6Hz, NCH₂Ar), 3.79 (3H, s, OCH₃), 3.82 (3H, s, OCH₃), 6.73 (1H, s, aryl CH), 6.95 (1H, s, aryl CH), 7.13-7.27 (5H, m, aryl CH); δ_C (100MHz, CDCl₃) 38.11, 50.80, 55.93, 56.05, 59.16, 62.55, 112.94, 113.86, 115.47, 126.30, 128.42, 129.08, 130.89, 138.34, 148.30, 148.57; *m/z* (ES) 380 (MH⁺, ⁷⁹Br, 95%), 382 (MH⁺, ⁸¹Br, 100%).

(2) Eschweiler-Clarke N-Methylation. A round-bottomed flask, equipped with a magnetic stirring bar, containing the secondary amine (1.0 equiv.) was charged with CHCl₃ (0.1M), a 37% aqueous solution of formaldehyde (1.15 equiv.) and formic acid (2.5 equiv.). The stirred solution was heated at 65°C for 3 hours, then cooled to room temperature and partitioned between CH₂Cl₂ and a saturated aqueous solution of K₂CO₃. The resulting two-phase mixture was separated and then the aqueous phase was extracted two times with CH₂Cl₂. The combined organic layers were washed (saturated aqueous NaCl), dried (K₂CO₃), filtered, concentrated *in vacuo* and chromatographed.

(S)-2-[(2-Bromobenzyl)-methylamino]-3-phenyl-propan-1-ol; 2a (Br). Colorless oil; yield: 93%; R_f 0.35 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3440m br,

3061m, 3025m, 2935s, 1602m, 1567m, 1495s, 1455s, 1353s, 1138s, 1026s, 744s, 700s; δ_H (500MHz, CDCl₃) 2.31 (3H, s, CH₃), 2.45 (1H, dd, J13, 9Hz, PhCHH'), 3.03-3.14 (2H, m, PhCHH' and NCH), 3.30 (1H, br s, OH), 3.39-3.49 (2H, m, CH₂OH), 3.77 (2H, s, NCH₂Ar), 7.12-7.34 (8H, m, aryl CH), 7.58 (1H, d, J8Hz, aryl CH); δ_C (100MHz, CDCl₃) 31.94, 35.40, 58.98, 61.01, 65.80, 125.12, 126.45, 127.49, 128.78, 129.12, 129.22, 131.46, 133.33, 137.94, 139.35; *m/z* (ES) 334 (MH⁺, ⁷⁹Br, 100%), 336 (MH⁺, ⁸¹Br, 95%).

(S)-2-[(2-Bromo-4,5-dimethoxybenzyl)-methylamino]-3-phenyl-propan-1-ol; 2. Colorless oil; yield: 86%; R_f 0.07 (SiO₂; Hexane: EtOAc; 4:1); [α]_D -2.6 (c=1.94, CH₂Cl₂); ν_{max} (thin film)/cm⁻¹ 3441m br, 2936s, 2848s, 1602m, 1506s, 1456s, 1382s, 1255s, 1214s, 1163s, 1032s, 911m, 802m, 733s, 700s; δ_H (500MHz, CDCl₃) 2.27 (3H, s, NCH₃), 2.39 (1H, dd, J13, 9Hz, PhCHH'), 2.96-3.04 (2H, m, PhCHH' and NCH), 3.18 (1H, br s, OH), 3.34 (1H, dd, J10.5, 4.5Hz, CHH'OH), 3.41 (1H, t, J10.5Hz, CHH'OH), 3.67 (2H, s, NCH₂Ar), 3.79 (3H, s, OCH₃), 3.80 (3H, s, OCH₃), 6.76 (1H, s, aryl CH), 6.98 (1H, s, aryl CH), 7.13-7.26 (5H, m, aryl CH); δ_C (100MHz, CDCl₃) 31.49, 35.05, 56.01, 56.08, 58.02, 60.57, 64.64, 113.72, 114.70, 115.61, 126.18, 128.51, 128.97, 129.71, 139.27, 148.26, 148.72; *m/z* (ES) 394 (MH⁺, ⁷⁹Br, 100%), 396 (MH⁺, ⁸¹Br, 95%); HRMS found 394.1001, C₁₉H₂₅BrNO₃ (MH⁺, ⁷⁹Br) requires 394.1018.

(S)-[1-Benzyl-2-(2-iodobenzyloxy)-ethyl]-(2-iodobenzyl)-methylamine; 3a. Colorless oil; yield: 100%; R_f 0.31 (SiO₂; Hexane: EtOAc; 9:1); [α]_D -12.5 (c=3.84, CH₂Cl₂); ν_{max} (thin film)/cm⁻¹ 3059m, 3025m, 2933s, 2853s, 2791m, 1603m, 1563s, 1495s, 1454s, 1436s, 1355s, 1264s, 1206m, 1122s, 1102s, 1043s, 1012s, 747s, 700s; δ_H (500MHz, CDCl₃) 2.45 (3H, s, CH₃), 2.92 (1H, dd, J13.5, 8Hz, PhCHH'), 3.00 (1H, dd, J13.5, 7Hz, PhCHH'), 3.27-3.33 (1H, m, NCH), 3.71 (1H, dd, J10, 4Hz, CHH'OCH₂Ar), 3.79 (1H, dd, J10, 6.5Hz, CHH'OCH₂Ar), 3.85-3.91 (2H, ABq, J15Hz, NCH₂Ar), 4.53 (2H, s, OCH₂Ar), 6.95 (1H, td, J7.5, 1.5Hz, aryl CH), 7.03 (1H, td, J7.5, 1.5Hz, aryl CH), 7.26-7.36 (7H, m, aryl CH), 7.40 (1H, t, J7.5Hz, aryl CH), 7.57 (1H, dd, J7.5, 1Hz, aryl CH), 7.85 (1H, d, J8Hz, aryl CH), 7.87 (1H, d, J8Hz, aryl CH); δ_C (125MHz, CDCl₃) 34.97, 36.98, 63.81, 64.53, 70.41, 76.91, 97.35, 99.95, 125.80, 127.84, 128.10, 128.18, 128.27, 128.54, 128.87, 129.22, 129.96, 138.86, 139.04, 140.18, 140.60, 141.79; *m/z* (ES) 598 (MH⁺, 100%); HRMS found 598.0086, C₂₂H₂₆I₂NO (MH⁺) requires 598.0104.

(S)-2-(2-Bromo-4,5-dimethoxybenzyl)-[1-(2-bromo-phenoxyethyl)-2-phenyl-ethyl]-methylamine; 3c. Colorless oil; yield: 100%; R_f 0.33 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3061m, 3024m, 2999m, 2934s, 2843s, 1602m, 1586m, 1573m, 1503s, 1481s, 1462s, 1442s, 1381s, 1276s, 1250s, 1209s, 1157s, 1051s, 1031s, 801m, 747s, 700m; δ_H (500MHz, CDCl₃) 2.49 (3H, s, NCH₃), 3.06 (1H, dd, J13.5, 7.5Hz, PhCHH'), 3.14 (1H, dd, J13.5, 7.5Hz, PhCHH'), 3.41-3.45 (1H, m, NCH), 3.73 (3H, s, OCH₃), 3.86 (1H, d, J14.5Hz, NCHH'Ar), 3.87 (3H, s, OCH₃), 4.01 (1H, d, J14.5Hz, NCHH'Ar), 4.13 (2H, d, J5Hz, CH₂OAr), 6.85-6.88 (2H, m, aryl CH), 6.92 (1H, s, aryl CH), 7.01 (1H, s, aryl CH), 7.20-7.31 (6H, m, aryl CH), 7.60 (1H, dd, J7.5, 1.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 35.07 (CH₂), 37.92, 56.30 & 56.47 (3 x CH₃), 58.63 (CH₂), 64.09 (CH), 68.27 (CH₂), 112.39 (quaternary), 112.83 & 112.97 (2 x CH), 113.87 (quaternary), 115.29, 122.00, 126.17, 128.53, 128.60 & 129.41 (6 x CH), 131.24 (quaternary), 133.50 (CH), 140.09, 148.27, 148.51 & 155.30 (4 x quaternary); *m/z* (ES) 548 (MH⁺, ⁷⁹Br ⁷⁹Br, 70%), 550 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 552 (MH⁺, ⁸¹Br ⁸¹Br, 80%); HRMS found 548.0419, C₂₅H₂₈Br₂NO₃ (MH⁺, ⁷⁹Br) requires 548.0436.

δ_H (500MHz, CDCl₃) 7.27 (1H, td, J7.5, 1.5Hz, aryl CH), 7.45 (1H, td, J7.5, 1.5Hz, aryl CH), 7.86 (1H, dd, J7.5, 1.5Hz, aryl CH), 7.93 (1H, dd, J8, 1Hz, aryl CH), 10.05 (1H, s, CHO); δ_C (125MHz, CDCl₃) 100.66, 128.66, 130.18, 135.03, 135.41, 140.57, 195.69; *m/z* (CI) 250 (MNH₃⁺, 100%), 232 (MH⁺, 25%). Found: C, 36.5; H, 1.85; I, 54.9%. C₈H₇IO requires C, 36.2; H, 2.15; I, 54.7%.

(S)-(2-Bromo-4,5-dimethoxybenzyl)-[1-(2-bromophenoxymethyl)-3-methyl-butyl]-methylamine; 3u. Colorless oil; yield: 100%; R_f 0.28 (SiO₂; Hexane: EtOAc; 4:1); $\nu_{\max}$ (thin film)/cm⁻¹ 3064m, 2951s, 2866s, 1587m, 1578m, 1504s, 1463s, 1382s, 1249s, 1211s, 1160s, 1031s, 802m, 748s; δ_H (500MHz, CDCl₃) 0.91 (3H, d, J 7Hz, CCH₃), 0.96 (3H, d, J 6.5Hz, CCH₃), 1.31-1.37 (1H, m, CHH'CH(CH₃)₂), 1.58-1.64 (1H, m, CHH'CH(CH₃)₂), 1.85-1.95 (1H, m, CH(CH₃)₂), 2.34 (3H, s, NCH₃), 3.19-3.24 (1H, m, NCH), 3.85 (6H, s, OCH₃), 3.86 (1H, d, J 14.5Hz, NCHH'Ar), 3.94 (1H, d, J 14.5Hz, NCHH'Ar), 4.00 (1H, dd, J 9.5, 4Hz, CHH'OAr), 4.16 (1H, dd, J 9.5, 6.5Hz, CHH'OAr), 6.83 (1H, td, J 7.5, 1Hz, aryl CH), 6.92 (1H, dd, J 8, 1.5Hz, aryl CH), 7.00 (1H, s, aryl CH), 7.15 (1H, s, aryl CH), 7.26 (1H, td, J 7.5, 1.5Hz, aryl CH), 7.54 (1H, dd, J 8, 1.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 22.59 & 23.77 (2 x CH₃), 25.29 (CH), 36.83 (CH₃), 38.63 (CH₂), 56.20 & 56.46 (2 x CH₃), 58.87 (CH₂), 59.69 (CH), 69.42 (CH₂), 112.38 (quaternary), 112.87 & 113.16 (2 x CH), 114.07 (quaternary), 115.51, 121.94 & 128.59 (3 x CH), 131.82 (quaternary), 133.55 (CH), 148.32, 148.52 & 155.59 (3 x quaternary); m/z (ES) 514 (MH⁺, ⁷⁹Br ⁷⁹Br, 40%), 516 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 518 (MH⁺, ⁸¹Br ⁸¹Br, 40%); HRMS found 514.0573, C₂₂H₃₀Br₂NO₃ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 514.0592.

(3) Reductive Alkylation of Secondary Amines.

A round-bottomed flask, equipped with a magnetic stirring bar, containing the secondary amine (1.0 equiv.), benzaldehyde (1.2 equiv.) and MeOH (0.1M) was charged with borane-pyridine complex (2.0 equiv., *ca.* 8M, contains excess pyridine). The solution was stirred at room temperature for 1-3 days (TLC), and the excess borane was quenched with the addition of an aqueous solution of HCl (2M, until pH 1-2). The mixture was concentrated *in vacuo* to remove the MeOH and distilled water was added. The aqueous solution was extracted three times with Et₂O, neutralized with an aqueous solution of NaOH (2M, until pH 10) and then extracted three times with CH₂Cl₂. The combined organic layers were washed (saturated aqueous NaCl), dried (K₂CO₃), filtered, concentrated *in vacuo* and chromatographed.

(1S,2S)-2-[(2-Bromo-benzyl)-methyl-amino]-1-phenyl-propan-1-ol; 2m. Colorless oil; yield: 95%; R_f 0.43 (SiO₂; Hexane: EtOAc; 4:1); $\nu_{\max}$ (thin film)/cm⁻¹ 3382m br, 3062m, 3029m, 2971s, 2856s, 2804m, 1568m, 1494m, 1455s, 1425s, 1372s, 1206s, 1149s, 1090s, 1027s, 756s, 701s; δ_H (500MHz, CDCl₃) 0.86 (3H, d, J 7Hz, CHCH₃), 2.27 (3H, s, NCH₃), 2.77-2.83 (1H, m, CHCH₃), 3.71-3.78 (2H, ABq, J 13.5Hz, NCH₂), 4.33 (1H, d, J 9.5Hz, PhCH), 5.06 (1H, br s, OH), 7.18 (1H, td, J 7.5, 1.5Hz, aryl CH), 7.26-7.42 (7H, m, aryl CH), 7.62 (1H, dd, J 8, 1Hz, aryl CH); δ_C (125MHz, CDCl₃) 7.43, 34.67, 58.61, 64.56, 74.79, 124.96, 127.22, 127.26, 127.58, 128.09, 128.89, 131.21, 133.06, 137.45, 141.89; m/z (ES) 334 (MH⁺, ⁷⁹Br, 95%), 336 (MH⁺, ⁸¹Br, 100%); HRMS found 334.0741, C₁₇H₂₁BrNO (MH⁺, ⁷⁹Br) requires 334.0728.

(S)-Benzyl-[1-benzyl-2-(2-bromobenzyloxy)-ethyl]-(2-bromobenzyl)-amine; 3j. Colorless oil; yield: 59%; R_f 0.43 (SiO₂; Hexane: EtOAc; 95:5); $\nu_{\max}$ (thin film)/cm⁻¹ 3083m, 3061s, 3026s, 2858s, 1602m, 1568m, 1494s, 1466s, 1453s, 1440s, 1358s, 1265m, 1205m, 1125s, 1073m, 1044s, 1027s, 749s, 699s; δ_H (500MHz, CDCl₃) 2.91 (1H, dd, J 13, 8Hz, PhCHH'C), 3.00 (1H, dd, J 13, 6.5Hz, PhCHH'C), 3.13-3.18 (1H, m, NCH), 3.68-3.71 (2H, m, CH₂OCH₂Ar), 3.85 (2H, s, NCH₂Ar), 3.90 (1H, d, J 15.5Hz, NCHH'Ar), 4.00 (1H, d, J 15.5Hz, NCHH'Ar), 4.49-4.54 (2H, ABq, J 13Hz, OCH₂Ar), 7.01-7.54 (18H, m, aryl CH); δ_C (100MHz, CDCl₃) 35.11, 54.16 & 55.06 (3 x CH₂), 60.23 (CH), 70.87 & 72.78 (2 x CH₂), 122.55 & 124.19 (2 x quaternary), 126.11, 126.98, 127.43, 127.54, 128.14, 128.37, 128.40, 128.78, 128.91, 129.07, 129.69, 130.55, 132.50 & 132.56 (14 x

CH), 138.04, 139.36, 140.18 & 140.27 (4 x quaternary); m/z (ES) 578 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 580 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 582 (MH⁺, ⁸¹Br ⁸¹Br, 55%); HRMS found 578.0713, C₃₀H₃₀Br₂NO (MH⁺, ⁷⁹Br ⁷⁹Br) requires 578.0694.

(S)-2-[(2-Bromobenzyl)-(2,4,6-trimethoxybenzyl)-amino]-3-phenylpropan-1-ol; 2k. Colorless oil; yield: 95%; R_f 0.23 (SiO₂; Hexane: EtOAc; 7:3); $\nu_{\max}$ (thin film)/cm⁻¹ 3471m br, 3061m, 3025m, 2999m, 2938s, 2838s, 1595s, 1497s, 1456s, 1418s, 1373s, 1320s, 1228s, 1205s, 1151s, 1043s, 952s, 813s, 750s, 701s; δ_H (500MHz, CDCl₃) 2.47 (1H, dd, J 13, 11Hz, PhCHH'), 2.92-2.98 (1H, m, NCH), 3.20-3.24 (1H, br m, CHH'OH), 3.27 (1H, dd, J 13, 3.5Hz, PhCHH'), 3.56 (1H, t, J 10.5Hz, CHH'OH), 3.70 (1H, br s, OH), 3.75 (1H, d, J 12Hz, NCHH'Ar), 3.79 (1H, d, J 14Hz, NCHH'Ar), 3.80 (3H, s, OCH₃), 3.81 (6H, s, OCH₃), 3.82 (1H, d, J 12Hz, NCHH'Ar), 3.89 (1H, d, J 14Hz, NCHH'Ar), 6.12 (2H, s, aryl CH), 7.03 (1H, td, J 8, 1.5Hz, aryl CH), 7.14-7.26 (6H, m, aryl CH), 7.34 (1H, dd, J 8, 1.5Hz, aryl CH), 7.46 (1H, dd, J 8, 1.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 31.84, 40.48 & 53.40 (3 x CH₂), 55.63 & 55.86 (2 x CH₃), 60.73 (CH₂), 61.98 & 90.63 (2 x CH), 107.23 & 124.50 (2 x quaternary), 126.10, 127.24, 128.37, 128.54, 129.21, 131.55 & 132.69 (7 x CH), 139.16, 139.78, 159.88 & 160.75 (4 x quaternary); m/z (ES) 500 (MH⁺, ⁷⁹Br, 100%), 502 (MH⁺, ⁸¹Br, 90%); HRMS found 500.1412, C₂₆H₃₁BrNO₄ (MH⁺, ⁷⁹Br) requires 500.1436.

(S)-5-[[1-Benzyl-2-(2-iodobenzyloxy)ethyl]-(2-iodobenzyl)-amino]-pentan-1-ol; 3l.¹⁸ Colorless oil; yield: 99%; R_f 0.22 (SiO₂; Hexane: EtOAc; 4:1); $\nu_{\max}$ (thin film)/cm⁻¹ 3383m br, 3059m, 3025m, 2932s, 2858s, 1602w, 1563m, 1495m, 1454s, 1435s, 1357s, 1244s, 1206m, 1132s, 1099s, 1044s, 1012s, 748s, 700s; δ_H (500MHz, CDCl₃) 1.26-1.51 (6H, m, CH₂), 1.75 (1H, br s, OH), 2.62-2.73 (2H, m, NCH₂), 2.86 (1H, dd, J 13.5, 8Hz, PhCHH'), 2.91 (1H, dd, J 13.5, 6.5Hz, PhCHH'), 3.12-3.28 (1H, m, NCH), 3.56 (2H, t, J 6.5Hz, CH₂OCH), 3.63 (1H, dd, J 10, 4.5Hz, CHH'OCH₂Ar), 3.70 (1H, dd, J 10, 6Hz, CHH'OCH₂Ar), 3.79-3.87 (2H, ABq, J 16Hz, NCH₂Ar), 4.43 (2H, s, OCH₂Ar), 6.89 (1H, td, J 7.5, 1.5Hz, aryl CH), 6.99 (1H, td, J 8.5, 1.5Hz, aryl CH), 7.16-7.36 (8H, m, aryl CH), 7.47 (1H, dd, J 7.5, 1Hz, aryl CH), 7.77 (1H, dd, J 8, 1Hz, aryl CH), 7.82 (1H, dd, J 8, 1Hz, aryl CH); δ_C (125MHz, CDCl₃) 23.39, 28.62, 32.63, 35.16, 50.67, 60.50, 61.97, 62.90, 70.84, 77.00, 97.37, 99.45, 125.89, 127.94, 128.20, 128.25, 128.57, 128.99, 129.43, 130.06, 138.89, 138.96, 140.37, 140.70, 142.64; m/z (ES) 670 (MH⁺, 100%); HRMS found 670.0697, C₂₈H₃₄I₂NO₂ (MH⁺) requires 670.0679.

Alkylation of Alcohols.

A round-bottomed flask, equipped with a magnetic stirring bar, containing the alcohol (1.0 equiv.) was charged with anhydrous THF (0.1M) and 95% NaH (1.1 equiv.) [Caution! Flammable solid, hydrogen gas evolved]. The stirred solution was heated at reflux for 30 minutes, then allowed to cool to room temperature and the benzyl bromide (1.2 equiv.) was added as a solution in anhydrous THF. The mixture was heated at reflux for 2-12 hours, cooled to room temperature and quenched by the addition of MeOH (1.0 equiv.). The mixture was concentrated *in vacuo*, partitioned between CH₂Cl₂ and an aqueous solution of Na₂CO₃ (1M). The resulting two-phase mixture was separated and then the aqueous phase was extracted two times with CH₂Cl₂. The combined organic layers were washed (saturated aqueous NaCl), dried (K₂CO₃), filtered, concentrated *in vacuo* and chromatographed.

(S)-[1-Benzyl-2-(2-bromo-4-fluorobenzyloxy)-ethyl]-(2-bromobenzyl)-methyl-amine; 3b. Colorless oil; yield: 52% (3 steps); R_f 0.31 (SiO₂; Hexane: EtOAc; 9:1); $\nu_{\max}$

(18 Tetrahydropyran-2-ol (2.5 equiv.; Acros) was used in place of a benzaldehyde.

(thin film)/cm⁻¹ 3062m, 3026m, 2855s, 1600s, 1488s, 1454m, 1354m, 1261m, 1231s, 1124s, 1030s, 859m, 815m, 750s, 699s; δ_{H} (500MHz, CDCl₃) 2.47 (3H, s, NCH₃), 2.91 (1H, dd, J13.5, 8.5Hz, PhCHH'), 3.02 (1H, dd, J13.5, 7Hz, PhCHH'), 3.26-3.31 (1H, m, NCH₃), 3.70 (1H, dd, J10, 4Hz, CHH'OCH₂Ar), 3.78 (1H, dd, J10, 6.5Hz, CHH'OCH₂Ar), 3.92-3.99 (2H, ABq, J15Hz, NCH₂Ar), 4.57 (2H, s, OCH₂Ar), 7.09 (1H, td, J8, 3Hz, aryl CH), 7.13 (1H, td, J7.5, 1.5Hz, aryl CH), 7.25-7.41 (8H, m, aryl CH), 7.54 (1H, dd, J8.5, 6.5Hz, aryl CH), 7.58 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 35.25 (CH₂), 37.85 (CH₃), 59.08 (CH₂), 65.10 (CH), 70.77 & 72.16 (2 x CH₂), 114.67 (d, J20.5Hz, CH), 119.82 (d, J24.5Hz, CH), 122.46 (d, J9Hz, quaternary), 124.35 (quaternary), 126.16, 127.39, 128.27, 128.52, 129.50, 130.13 (d, J8.5Hz), 130.56 & 132.67 (8 x CH), 133.98 (d, J4Hz, quaternary), 139.27 & 140.40 (2 x quaternary), 161.71 (d, J249Hz, quaternary); m/z (ES) 520 (MH⁺, ⁷⁹Br ⁷⁹Br, 45%), 522 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 524 (MH⁺, ⁸¹Br ⁸¹Br, 45%); HRMS found 520.0311, C₂₄H₂₅Br₂FNO (MH⁺, ⁷⁹Br ⁷⁹Br) requires 520.0287.

(S)-[1-Benzyl-2-[2-(2-bromophenyl)-ethoxy]-ethyl]-(2-bromobenzyl)-methyl-amine; 3d.¹⁹ Colorless oil; yield: 31%; R_f 0.21 (SiO₂; Hexane: EtOAc; 95:5); ν_{max} (thin film)/cm⁻¹ 3061m, 3025m, 2931s, 2858s, 2792m, 1592m, 1567m, 1495m, 1472s, 1440s, 1160s, 1117s, 1024s, 749s, 700s; δ_{H} (500MHz, CDCl₃) 2.31 (3H, s, CH₃), 2.75 (1H, dd, J13.5, 8.5Hz, PhCHH'), 2.82 (1H, dd, J13.5, 6.5Hz, PhCHH'), 3.03 (2H, t, J7Hz, OCH₂CH₂Ar), 3.03-3.07 (1H, m, NCH₃), 3.49 (2H, d, J5Hz, CH₂O), 3.54-3.64 (2H, m, CH₂O), 3.79 (2H, s, NCH₂Ar), 7.01-7.29 (11H, m, aryl CH), 7.47 (1H, dd, J8, 1Hz, aryl CH), 7.51 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 34.92 & 37.08 (2 x CH₂), 38.05 (CH₃), 58.94 (CH₂), 65.12 (CH), 70.46 & 70.68 (2 x CH₂), 124.38 & 124.82 (2 x quaternary), 125.98, 127.33, 127.49, 128.16, 128.18, 128.40, 129.48, 130.65, 131.63, 132.63 & 132.89 (11 x CH), 138.66, 139.42 & 140.58 (3 x quaternary); m/z (ES) 516 (MH⁺, ⁷⁹Br ⁷⁹Br, 35%), 518 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 520 (MH⁺, ⁸¹Br ⁸¹Br, 40%); HRMS found 516.0548, C₂₅H₂₈Br₂NO (MH⁺, ⁷⁹Br ⁷⁹Br) requires 516.0537.

(S)-[1-Benzyl-2-(2-bromobenzyloxy)-ethyl]-(2-bromo-4,5-dimethoxy-benzyl)-methyl-amine; 3e. White solid; yield: 97%; m.p. 77.5-78.5°C; R_f 0.42 (SiO₂; Hexane: EtOAc; 4:1); [α]_D -19.5 (c=1.21, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 3060m, 3025m, 2999m, 2933s, 2847s, 2790m, 1602m, 1504s, 1464s, 1437s, 1381s, 1356s, 1256s, 1209s, 1156s, 1125s, 1107s, 1029s, 802s, 750s, 700s; δ_{H} (500MHz, CDCl₃) 2.36 (3H, s, NCH₃), 2.82-2.92 (2H, m, PhCH₂), 3.22-3.27 (1H, m, NCH₃), 3.63 (3H, s, OCH₃), 3.64 (1H, dd, J10, 4.5Hz, CHH'OCH₂Ar), 3.74 (1H, d, J14Hz, NCHH'Ar), 3.75 (1H, dd, J10, 6.5Hz, CHH'OCH₂Ar), 3.84 (3H, s, OCH₃), 3.87 (1H, d, J14Hz, NCHH'Ar), 4.56 (2H, s, OCH₂Ar), 6.87 (1H, s, aryl CH), 6.95 (1H, s, aryl CH), 7.13-7.32 (7H, m, aryl CH), 7.52-7.54 (2H, m, aryl CH); δ_{C} (125MHz, CDCl₃) 34.81, 37.17, 55.86, 56.12, 57.90, 64.21, 70.42, 72.49, 112.69, 113.41, 115.06, 122.36, 125.81, 127.36, 128.23, 128.75, 128.88, 129.19, 131.20, 132.36, 137.84, 140.36, 148.09, 148.45; m/z (ES) 562 (MH⁺, ⁷⁹Br ⁷⁹Br, 70%), 564 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 566 (MH⁺, ⁸¹Br ⁸¹Br, 60%); HRMS found 562.0928, C₂₆H₃₀Br₂NO₃ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 562.0952.

(S)-[1-Benzyl-2-(1-bromo-naphthalen-2-ylmethoxy)-ethyl]-(2-bromo-benzyl)-methyl-amine; 3f. Colorless oil; yield: 82% (3 steps); R_f 0.41 (SiO₂; Hexane: EtOAc; 9:1); ν_{max} (thin film)/cm⁻¹ 3061m, 3026m, 2854s, 2793m, 1601m, 1566m, 1502s, 1440s, 1325s, 1258s, 1122s, 1025s, 968s, 813s, 766s, 749s, 700s, 657s; δ_{H} (500MHz, CDCl₃) 2.32 (3H, s, NCH₃), 2.77 (1H, dd, J13.5, 8Hz, PhCHH'), 2.85 (1H, dd,

J13.5, 6.5Hz, PhCHH'), 3.14-3.20 (1H, m, NCH₃), 3.58 (1H, dd, J10, 4Hz, CHH'OCH₂Ar), 3.64 (1H, dd, J10, 6.5Hz, CHH'OCH₂Ar), 3.80-3.89 (2H, ABq, J15.5Hz, NCH₂Ar), 4.69 (2H, s, OCH₂Ar), 6.95 (1H, t, J7.5Hz, aryl CH), 7.08-7.48 (10H, m, aryl CH), 7.60 (1H, d, J8.5Hz, aryl CH), 7.68 (2H, d, J8.5Hz, aryl CH), 8.24 (1H, d, J8.5Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 35.50 (CH₂), 38.00 (CH₃), 59.33 (CH₂), 65.34 (CH), 70.98 & 73.70 (2 x CH₂), 122.40 & 124.57 (2 x quaternary), 126.30, 126.73, 127.27, 127.56, 127.72, 128.02, 128.41, 128.53, 128.68, 129.69 & 130.76 (11 x CH), 132.42 (quaternary), 132.82 (CH), 134.26, 136.49, 139.53 & 140.63 (4 x quaternary); m/z (ES) 552 (MH⁺, ⁷⁹Br ⁷⁹Br, 35%), 554 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 556 (MH⁺, ⁸¹Br ⁸¹Br, 35%); HRMS found 552.0511, C₂₈H₂₈Br₂NO (MH⁺, ⁷⁹Br ⁷⁹Br) requires 552.0537.

(S)-[1-Benzyl-2-(4-bromo-thiophen-3-ylmethoxy)-ethyl]-(2-bromo-benzyl)-methyl-amine; 3g. Colorless oil; yield: 88% (3 steps); R_f 0.37 (SiO₂; Hexane: EtOAc; 9:1); ν_{max} (thin film)/cm⁻¹ 3110m, 3060m, 3025m, 2855s, 2794m, 1602m, 1566m, 1495s, 1453s, 1440s, 1350m, 1322m, 1258m, 1162m, 1117s, 1024s, 987s, 852m, 793s, 750s, 700s; δ_{H} (500MHz, CDCl₃) 2.36 (3H, s, NCH₃), 2.81 (1H, dd, J13.5, 8Hz, PhCHH'), 2.89 (1H, dd, J13.5, 6.5Hz, PhCHH'), 3.13-3.18 (1H, m, NCH₃), 3.57 (1H, dd, J10, 4.5Hz, CHH'OCH₂Ar), 3.66 (1H, dd, J10, 6.5Hz, CHH'OCH₂Ar), 3.80-3.87 (2H, ABq, J15Hz, NCH₂Ar), 4.38-4.44 (2H, ABq, J13Hz, OCH₂Ar), 7.03 (1H, td, J8, 1.5Hz, aryl CH), 7.11-7.29 (9H, m, aryl CH), 7.47 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 35.13 (CH₂), 37.72 (CH₃), 58.96 (CH₂), 64.97 (CH), 68.49 & 70.56 (2 x CH₂), 110.86 (quaternary), 123.61 & 123.95 (2 x CH), 124.47 (quaternary), 126.20, 127.47, 128.35, 128.59, 129.62, 130.75 & 132.77 (7 x CH), 138.31, 139.44 & 140.62 (3 x quaternary); m/z (ES) 508 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 510 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 512 (MH⁺, ⁸¹Br ⁸¹Br, 60%); HRMS found 507.9922, C₂₂H₂₄Br₂NOS (MH⁺, ⁷⁹Br ⁷⁹Br) requires 507.9945.

(S)-[2-Bromobenzyl]-[1-(2-bromo-5-chloro-benzo[b]thiophen-3-ylmethoxymethyl)-2-phenyl-ethyl]-methyl-amine; 3h. Colorless oil; yield: 85% (3 steps); R_f 0.66 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3060m, 3025m, 2932s, 2858s, 2791m, 1585m, 1557m, 1495m, 1453s, 1422s, 1354m, 1250m, 1146m, 1113s, 1079s, 1043s, 1025s, 947m, 855m, 800s, 750s, 700s; δ_{H} (500MHz, CDCl₃) 2.31 (3H, s, NCH₃), 2.73 (1H, dd, J13.5, 8.5Hz, PhCHH'), 2.86 (1H, dd, J13.5, 6.5Hz, PhCHH'), 3.08-3.13 (1H, m, NCH₃), 3.54 (1H, dd, J10.5, 4.5Hz, CHH'OCH₂Ar), 3.61 (1H, dd, J10.5, 7Hz, CHH'OCH₂Ar), 3.77 (2H, s, NCH₂Ar), 4.62-4.69 (2H, ABq, J12Hz, OCH₂Ar), 7.03 (1H, td, J7.5, 2Hz, aryl CH), 7.12-7.26 (7H, m, aryl CH), 7.30 (1H, dd, J8.5, 2Hz, aryl CH), 7.46 (1H, dd, J8, 1Hz, aryl CH), 7.61 (1H, d, J8.5Hz, aryl CH), 7.91 (1H, d, J2Hz, aryl CH); δ_{C} (100MHz, CDCl₃) 34.70 (CH₂), 37.83 (CH₃), 58.72 (CH₂), 64.90 (CH), 65.58 & 70.08 (2 x CH₂), 122.36 & 122.78 (2 x CH₂), 123.03 & 124.37 (2 x quaternary), 125.45, 126.04, 127.32, 128.20, 128.41, 129.40 & 130.67 (7 x CH), 131.40 & 132.04 (2 x quaternary), 132.60 (CH), 137.88, 139.10, 139.47 & 140.28 (4 x quaternary); m/z (ES) 592 (MH⁺, ⁷⁹Br ⁷⁹Br, 35%), 594 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 596 (MH⁺, ⁸¹Br ⁸¹Br, 65%); HRMS found 591.9684, C₂₆H₂₅Br₂ClNOS (MH⁺, ⁷⁹Br ⁷⁹Br) requires 591.9712.

(S)-[1-Benzyl-2-(2-bromopyridin-3-ylmethoxy)-ethyl]-(2-bromobenzyl)-methyl-amine; 3i. Colorless oil; R_f 0.39 (SiO₂; Hexane: EtOAc; 9:1); ν_{max} (thin film)/cm⁻¹ 3060m, 3025m, 2858s, 1580m, 1561s, 1495m, 1440s, 1405s, 1349s, 1262m, 1188m, 1125s, 1052s, 1025s, 794m, 750s, 700s; δ_{H} (500MHz, CDCl₃) 2.40 (3H, s, NCH₃), 2.82 (1H, dd, J13.5, 8.5Hz, PhCHH'), 2.96 (1H, dd, J13.5, 6.5Hz, PhCHH'), 3.19-3.24 (1H, m, NCH₃), 3.66 (1H, dd, J10, 4Hz, CHH'OCH₂Ar), 3.74 (1H, dd, J10, 7Hz, CHH'OCH₂Ar), 3.84-3.91 (2H, ABq, J15Hz,

(19) A mixture of (S)-2-[(2-bromobenzyl)-methylamino]-3-phenyl-propan-1-ol (**2a**), 1-bromo-2-(2-iodoethyl)-benzene (5.0 equiv.) and Ag₂O (3.0 equiv.) were heated to 90°C for 60 hours.

NCH₂Ar), 4.49 (2H, s, OCH₂Ar), 7.10 (1H, t, *J*8Hz, aryl CH), 7.22-7.38 (8H, m, aryl CH), 7.54 (1H, d, *J*8Hz, aryl CH), 7.84 (1H, dd, *J*8, 1Hz, aryl CH), 8.31 (1H, dd, *J*5, 2Hz, aryl CH); δ_c (100MHz, CDCl₃) 35.12 (CH₂), 37.75 (CH₃), 59.12 (CH₂), 65.03 (CH), 71.05 & 71.29 (2 x CH₂), 123.13 (CH), 124.32 (quaternary), 126.22, 127.42, 128.35, 128.55, 129.41, 130.53 & 132.67 (7 x CH), 135.60 (quaternary), 136.87 (CH), 140.15 & 141.47 (2 x quaternary), 148.67 (CH), 149.85 (quaternary); *m/z* (ES) 503 (MH⁺, ⁷⁹Br ⁷⁹Br, 75%), 505 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 507 (MH⁺, ⁸¹Br ⁸¹Br, 75%); HRMS found 503.0309, C₂₃H₂₅Br₂N₂O (MH⁺, ⁷⁹Br ⁷⁹Br) requires 503.0333.

(S)-[1-Benzyl-2-(2-bromobenzyloxy)-ethyl]-(2-bromobenzyl)-(2,4,6-trimethoxybenzyl)-amine; 3k. Colorless oil; yield: 89%; *R_f* 0.27 (SiO₂; Hexane: EtOAc; 9:1); ν_{max} (thin film)/cm⁻¹ 3060m, 3024m, 2997m, 2935s, 2836s, 1608s, 1496s, 1465s, 1438s, 1417s, 1226s, 1204s, 1151s, 1133s, 1061s, 1043s, 1025s, 952m, 812m, 750s, 700s; δ_H (500MHz, CDCl₃) 2.91 (1H, dd, *J*13.5, 8Hz, PhCHH'), 3.01 (1H, dd, *J*13.5, 7Hz, PhCHH'), 3.21-3.26 (1H, m, NCH), 3.66-3.74 (2H, m, C(2)H₂), 3.68 (6H, s, OCH₃), 3.76-3.82 (2H, ABq, *J*10Hz, NCH₂Ar), 3.79 (3H, s, OCH₃), 3.92-4.00 (2H, ABq, *J*16Hz, NCH₂Ar), 6.03 (2H, s, aryl CH), 6.97 (1H, td, *J*7.5, 1.5Hz, aryl CH), 7.05-7.53 (12H, m, aryl CH); δ_c (100MHz, CDCl₃) 35.25, 43.61 & 54.29 (3 x CH₂), 55.58 (CH₃), 61.17 (CH), 71.24 & 72.47 (2 x CH₂), 90.36 (CH), 108.41, 122.12 & 123.63 (3 x quaternary), 125.58, 126.68, 127.47, 127.49, 128.13, 128.61, 128.88, 129.48, 131.03, 131.85 & 132.31 (11 x CH), 138.49, 140.75, 141.21, 160.09 & 160.52 (5 x quaternary); *m/z* (ES) 668 (MH⁺, ⁷⁹Br ⁷⁹Br, 60%), 670 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 672 (MH⁺, ⁸¹Br ⁸¹Br, 55%); HRMS found 668.1040, C₃₃H₃₆Br₂NO₄ (MH⁺, ⁷⁹Br) requires 668.1011.

(1S,2S)-(2-Iodobenzyl)-[2-(2-iodobenzyloxy)-1-methyl-2-phenyl-ethyl]-methylamine; 3m. Colorless oil; yield: 88%; *R_f* 0.31 (SiO₂; Hexane: EtOAc; 19:1); ν_{max} (thin film)/cm⁻¹ 3058s, 3027m, 2966s, 2932s, 2866s, 2792s, 1563s, 1436s, 1344s, 1206s, 1087s, 1012s, 748s, 701s; δ_H (500MHz, CDCl₃) 0.90 (3H, d, *J*7Hz, CHCH₃), 2.33 (3H, s, NCH₃), 3.17 (1H, dq, *J*8.5, 7Hz, CHCH₃), 3.81-3.93 (2H, ABq, *J*15Hz, NCH₂), 4.29-4.35 (2H, ABq, *J*12.5Hz, OCH₂), 4.45 (1H, d, *J*8.5Hz, PhCH), 6.90 (1H, td, *J*8, 2Hz, aryl CH), 6.96 (1H, td, *J*8, 1.5Hz, aryl CH), 7.24 (1H, td, *J*7.5, 1Hz, aryl CH), 7.28-7.38 (6H, m, aryl CH), 7.43 (1H, dd, *J*8, 1.5Hz, aryl CH), 7.62 (1H, d, *J*7Hz, aryl CH), 7.78 (2H, td, *J*8, 1Hz, aryl CH); δ_c (100MHz, CDCl₃) 14.40 (CCH₃), 36.56 (NCH₃), 63.93 (NCH), 65.40 (NCH₂), 74.91 (OCH₂), 85.37 (OCH), 97.89 & 100.21 (2 x CI), 127.93, 128.07, 128.35, 128.42, 128.52, 129.05, 129.32, 130.28, 139.08 & 139.31 (10 x CH), 140.86, 141.21 & 142.64 (3 x quaternary); *m/z* (ES) 598 (MH⁺, 100%); HRMS found 598.0082, C₂₄H₂₆I₂NO (MH⁺) requires 598.0104. Found: C, 48.4; H, 4.30; I, 42.4; N, 2.3%. C₂₄H₂₅I₂NO requires C, 48.3; H, 4.20; I, 42.5; N, 2.4%.

(1S,2S)-(2-Bromobenzyl)-[2-(2-bromobenzyloxy)-1-methyl-2-phenyl-ethyl]-methylamine; 3m (Br). Colorless oil; yield: 95%; *R_f* 0.22 (SiO₂; Hexane: EtOAc; 9:1); $[\alpha]_D^{25} +363.9$ (c=2.35, CH₂Cl₂); ν_{max} (thin film)/cm⁻¹ 3061m, 2967m, 2933m, 2869m, 1568m, 1440s, 1345m, 1205m, 1090s, 1026s, 749s, 702s; δ_H (500MHz, CDCl₃) 0.89 (3H, d, *J*7Hz, CHCH₃), 2.34 (3H, s, NCH₃), 3.16 (1H, q, *J*7Hz, CHCH₃), 3.88-3.99 (2H, ABq, *J*15Hz, NCH₂), 4.37-4.43 (2H, ABq, *J*13Hz, OCH₂), 4.44 (1H, d, *J*8.5Hz, PhCH), 7.05 (1H, t, *J*7.5Hz, aryl CH), 7.11 (1H, t, *J*7.5Hz, aryl CH), 7.21 (1H, t, *J*7.5Hz, aryl CH), 7.23-7.36 (7H, m, aryl CH), 7.48-7.49 (2H, m, aryl CH), 7.65 (1H, d, *J*7.5Hz, aryl CH); δ_c (100MHz, CDCl₃) 14.20 (CCH₃), 36.79 (NCH₃), 60.24 (NCH₂), 64.04 (NCH), 70.28 (OCH₂), 85.36 (OCH), 122.68 & 124.36 (2 x CBr), 127.34, 127.54, 127.94,

128.00, 128.11, 128.59, 128.87, 129.60, 130.60, 132.52 & 132.67 (11 x CH), 138.42, 139.99 & 140.99 (3 x quaternary); *m/z* (ES) 502 (MH⁺, ⁷⁹Br ⁷⁹Br, 63%), 504 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 506 (MH⁺, ⁸¹Br ⁸¹Br, 76%); HRMS found 502.0404, C₂₄H₂₆Br₂NO (MH⁺, ⁷⁹Br ⁷⁹Br) requires 502.0387. Found: C, 57.2; H, 5.15; Br, 31.6; N, 2.7%. C₂₄H₂₅Br₂NO requires C, 57.3; H, 5.00; Br, 31.8; N, 2.8%.

(1S,2S)-(2-Bromo-5-chlorobenzyl)-[2-(2-bromo-5-chlorobenzyloxy)-1-methyl-2-phenyl-ethyl]-methylamine; 3n. Colorless oil; yield: 92%; *R_f* 0.32 (SiO₂; Hexane: EtOAc; 98:2); ν_{max} (thin film)/cm⁻¹ 2929m, 2869m, 1584w, 1453s, 1381m, 1345m, 1202m, 1096s, 1026s, 878m, 810s, 759m, 702s; δ_H (500MHz, CDCl₃) 0.94 (3H, d, *J*7Hz, CHCH₃), 2.39 (3H, s, NCH₃), 3.17 (1H, q, *J*7Hz, CHCH₃), 3.89-4.03 (2H, ABq, *J*16Hz, NCH₂), 4.36-4.42 (2H, ABq, *J*14.5Hz, OCH₂), 4.46 (1H, d, *J*8Hz, PhCH), 7.07 (1H, dd, *J*8.5, 2.5Hz, aryl CH), 7.12 (1H, dd, *J*8.5, 2.5Hz, aryl CH), 7.32-7.44 (7H, m, aryl CH), 7.57 (1H, d, *J*2Hz, aryl CH), 7.71 (2H, d, *J*2Hz, aryl CH); δ_c (100MHz, CDCl₃) 14.00, 36.42, 60.09, 63.90, 69.69, 85.37, 119.89, 121.56, 127.57, 128.02, 128.49, 128.64, 129.00, 129.91, 133.28, 133.37, 133.57, 133.63, 139.92, 140.24, 141.67; *m/z* (ES) 570 (MH⁺, ⁷⁹Br ⁷⁹Br ³⁵Cl ³⁵Cl, 62%), 572 (MH⁺, 100%), 573 (MH⁺, 40%), 574 (MH⁺, 79%), 575 (MH⁺, 38%), 576 (MH⁺, 55%); HRMS found 569.9586, C₂₄H₂₄Br₂Cl₂NO (MH⁺, ⁷⁹Br ³⁵Cl ³⁵Cl) requires 569.9601.

(R)-[2-(2-Bromobenzyloxy)-1-phenyl-ethyl]-(2-bromo-4,5-dimethoxy-benzyl)-methylamine; 3o. Colorless oil; *R_f* 0.48 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3060m, 2933s, 2844s, 1601m, 1568m, 1503s, 1438s, 1380s, 1256s, 1209s, 1157s, 1105s, 1028s, 800m, 751s, 702s; δ_H (500MHz, CDCl₃) 2.25 (3H, s, NCH₃), 3.62-3.69 (2H, ABq, *J*14.5Hz, NCH₂Ar), 3.80 (3H, s, OCH₃), 3.84 (3H, s, OCH₃), 3.89 (1H, dd, *J*10, 5.5Hz, PhCH), 3.96 (1H, t, *J*6Hz, CHH'OCH₂Ar), 4.09 (1H, dd, *J*10, 7Hz, CHH'OCH₂Ar), 4.60 (2H, s, OCH₂Ar), 6.97 (1H, s, aryl CH), 7.11 (1H, td, *J*8, 2Hz, aryl CH), 7.13 (1H, s, aryl CH), 7.24-7.42 (7H, m, aryl CH), 7.50 (1H, dd, *J*8, 2Hz, aryl CH); δ_c (100MHz, CDCl₃) 39.00, 56.27 & 56.48 (3 x CH₃), 58.47 (CH₂), 67.26 (CH), 72.18 & 72.75 (2 x CH₂), 113.33 (CH), 114.02 (quaternary), 115.39 (CH), 122.65 (quaternary), 127.52, 127.54, 128.39, 128.70, 129.00 & 129.12 (6 x CH), 131.07 (quaternary), 132.55 (CH), 137.80, 139.46, 148.36 & 148.52 (4 x quaternary); *m/z* (ES) 548 (MH⁺, ⁷⁹Br ⁷⁹Br, 45%), 550 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 552 (MH⁺, ⁸¹Br ⁸¹Br, 50%); HRMS found 548.0414, C₂₅H₂₈Br₂NO₃ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 548.0436.

(S)-[1-(2-Bromobenzyloxymethyl)-2,2-dimethyl-propyl]-(2-bromo-4,5-dimethoxy-benzyl)-methylamine; 3p. Colorless oil; *R_f* 0.45 (SiO₂; Hexane: EtOAc; 4:1); δ_H (500MHz, CDCl₃) 1.02 (9H, s, C(CH₃)₃), 2.41 (3H, s, NCH₃), 2.74 (1H, dd, *J*9.5, 3.5Hz, NCH), 3.82 (1H, d, *J*15Hz, NCHH'Ar), 3.88 (6H, s, OCH₃), 3.89 (1H, dd, *J*13.5, 3.5Hz, CHH'OCH₂Ar), 3.99 (1H, dd, *J*13.5, 9.5Hz, CHH'OCH₂Ar), 4.03 (1H, d, *J*15Hz, NCHH'Ar), 4.62-4.68 (2H, ABq, *J*13Hz, OCH₂Ar), 7.01 (1H, s, aryl CH), 7.18 (1H, td, *J*7.5, 1.5Hz, aryl CH), 7.32 (1H, s, aryl CH), 7.37 (1H, td, *J*7.5, 1Hz, aryl CH), 7.57 (1H, dd, *J*8, 1Hz, aryl CH), 7.68 (1H, dd, *J*8, 1Hz, aryl CH); δ_c (100MHz, CDCl₃) 28.59, 35.87, 40.48, 56.12, 56.42, 60.82, 69.28, 71.62, 72.74, 112.80, 113.62, 115.42, 122.36, 127.69, 128.90, 128.99, 132.43, 132.55, 138.27, 148.14, 148.61; *m/z* (ES) 528 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 530 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 532 (MH⁺, ⁸¹Br ⁸¹Br, 50%); HRMS found 528.0725, C₂₃H₃₂Br₂NO₃ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 528.0749.

(S)-[2-(2-Bromo-benzyloxy)-1-cyclohexylmethyl-ethyl]-(2-bromo-4,5-dimethoxy-benzyl)-methylamine; 3q. Colorless oil; yield: 68% (3 steps); *R_f* 0.51 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3068m, 2997m, 2921s, 2848s, 1602m, 1569m, 1502s, 1463s,

1438s, 1380s, 1356s, 1255s, 1209s, 1155s, 1124s, 1104s, 1030s, 801s, 750s; δ_{H} (500MHz, CDCl_3) 0.83-1.68 (13H, m, $\text{C}_6\text{H}_{11}\text{CH}_2$), 2.26 (3H, s, NCH_3), 3.03-3.07 (1H, m, NCH), 3.52 (1H, dd, J10, 4.5Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.73 (1H, d, J14.5Hz, $\text{NCHH}'\text{Ar}$), 3.75 (1H, dd, J10, 7Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.82 (1H, d, J14.5Hz, $\text{NCHH}'\text{Ar}$), 3.83 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 4.59 (2H, s, OCH_2Ar), 6.98 (1H, s, aryl CH), 7.12 (1H, s, aryl CH), 7.14 (1H, td, J8, 1.5Hz, aryl CH), 7.32 (1H, td, J7.5, 1Hz, aryl CH), 7.53 (1H, dd, J8, 1Hz, aryl CH), 7.57 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 26.73, 26.83, 26.93, 33.21 & 34.33 (5 x CH_2), 34.68 (CH), 36.64 (CH_3), 36.85 (CH_2), 56.02 & 56.29 (2 x CH_3), 58.38 (CH_2), 59.21 (CH), 71.67 & 72.60 (2 x CH_2), 112.81 (CH), 113.74 (quaternary), 115.16 (CH), 122.28 (quaternary), 127.33, 128.66 & 128.78 (3 x CH), 131.60 (quaternary), 132.29 (CH), 137.92, 147.99 & 148.27 (3 x quaternary); m/z (ES) 568 (MH^+ , ^{79}Br ^{79}Br , 50%), 570 (MH^+ , ^{79}Br ^{81}Br , 100%), 572 (MH^+ , ^{81}Br ^{81}Br , 55%); HRMS found 568.1038, $\text{C}_{26}\text{H}_{36}\text{Br}_2\text{NO}_3$ (MH^+ , ^{79}Br ^{79}Br) requires 568.1062.

(S)-[1-(2-Bromobenzyloxymethyl)-3-methyl-butyl]-(2-bromo-4,5-dimethoxy-benzyl)-methyl-amine; 3r. Colorless oil; yield: 74% (3 steps); R_f 0.49 (SiO_2 ; Hexane: EtOAc; 4:1); ν_{max} (thin film)/ cm^{-1} 3070m, 2928s, 2848s, 1602m, 1569m, 1503s, 1464s, 1438s, 1381s, 1357m, 1256s, 1209s, 1154s, 1123s, 1102s, 1030s, 801m, 751s; δ_{H} (500MHz, CDCl_3) 0.89 (3H, d, J7Hz, CCH_3), 0.93 (3H, d, J7Hz, CCH_3), 1.19-1.23 (1H, m, $\text{CHH}'\text{CH}(\text{CH}_3)_2$), 1.45-1.51 (1H, m, $\text{CHH}'\text{CH}(\text{CH}_3)_2$), 1.78-1.84 (1H, m, $\text{CH}(\text{CH}_3)_2$), 2.27 (3H, s, NCH_3), 2.99-3.02 (1H, m, NCH), 3.54 (1H, dd, J9.5, 4Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.73-3.84 (2H, ABq, J15Hz, NCH_2Ar), 3.76 (1H, dd, J9.5, 8Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.81 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 4.59 (2H, s, OCH_2Ar), 6.98 (1H, s, aryl CH), 7.14 (1H, t, J8Hz, aryl CH), 7.15 (1H, s, aryl CH), 7.32 (1H, t, J7.5Hz, aryl CH), 7.53 (1H, d, J8Hz, aryl CH), 7.58 (1H, d, J8Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 22.05 & 23.16 (2 x CH_3), 24.75 (CH), 36.08 (CH_3), 37.78 (CH_2), 55.36 & 55.68 (2 x CH_3), 57.93 (CH_2), 59.53 (CH), 71.09 & 72.09 (2 x CH_2), 112.23 (CH), 113.10 (quaternary), 114.63 (CH), 121.73 (quaternary), 126.81, 128.13 & 128.25 (3 x CH), 131.05 (quaternary), 131.73 (CH), 137.38, 147.49 & 147.80 (3 x quaternary); m/z (ES) 528 (MH^+ , ^{79}Br ^{79}Br , 45%), 530 (MH^+ , ^{79}Br ^{81}Br , 100%), 532 (MH^+ , ^{81}Br ^{81}Br , 50%); HRMS found 528.0760, $\text{C}_{23}\text{H}_{32}\text{Br}_2\text{NO}_3$ (MH^+ , ^{79}Br ^{79}Br) requires 528.0749.

(R)-[1-(2-Bromo-benzyloxymethyl)-propyl]-(2-bromo-4,5-dimethoxy-benzyl)-methyl-amine; 3s. Colorless oil; yield: 62% (3 steps); R_f 0.35 (SiO_2 ; Hexane: EtOAc; 4:1); ν_{max} (thin film)/ cm^{-1} 3069m, 2931s, 2845s, 1602m, 1569m, 1503s, 1464s, 1437s, 1380s, 1356m, 1255s, 1207s, 1153s, 1123s, 1103s, 1028s, 800m, 751s; δ_{H} (500MHz, CDCl_3) 1.00 (3H, t, J7.5Hz, CH_2CH_3), 1.49-2.03 (2H, m, CH_2CH_3), 2.28 (3H, s, NCH_3), 2.78-2.83 (1H, m, NCH), 3.57 (1H, dd, J10, 5Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.75 (1H, d, J13.5Hz, $\text{NCHH}'\text{Ar}$), 3.77 (1H, dd, J10, 3Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.80 (1H, d, J13.5Hz, $\text{NCHH}'\text{Ar}$), 3.82 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 4.58 (2H, s, OCH_2Ar), 6.98 (1H, s, aryl CH), 7.12 (1H, td, J8, 1.5Hz, aryl CH), 7.16 (1H, s, aryl CH), 7.30 (1H, td, J7.5, 1.5Hz, aryl CH), 7.51 (1H, dd, J7.5, 1Hz, aryl CH), 7.55 (1H, d, J7.5Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 11.61 (CH_3), 21.60 (CH_2), 36.25, 55.40 & 55.64 (3 x CH_3), 57.86 (CH_2), 63.41 (CH), 70.60 & 72.03 (2 x CH_2), 112.27 (CH), 113.07 (quaternary), 114.59 (CH), 121.71 (quaternary), 126.77, 128.10 & 128.22 (3 x CH), 131.00 (quaternary), 131.70 (CH), 137.34, 147.47 & 147.77 (3 x quaternary); m/z (ES) 500 (MH^+ , ^{79}Br ^{79}Br , 80%), 502 (MH^+ , ^{79}Br ^{81}Br , 100%), 504 (MH^+ , ^{81}Br ^{81}Br , 70%); HRMS found 500.0414, $\text{C}_{21}\text{H}_{28}\text{Br}_2\text{NO}_3$ (MH^+ , ^{79}Br ^{79}Br) requires 500.0436.

(R)-[2-(2-Bromo-benzyloxy)-1-methyl-ethyl]-(2-bromo-4,5-dimethoxy-benzyl)-methyl-amine; 3t. Colorless oil; R_f 0.17 (SiO_2 ; Hexane: EtOAc; 4:1); ν_{max} (thin film)/ cm^{-1} 3069m, 2933s, 2845s, 1602m, 1569m, 1503s, 1464s, 1438s, 1380s, 1256s, 1207s, 1156s, 1123s, 1102m, 1029s, 801m, 751s; δ_{H} (500MHz, CDCl_3) 1.11 (3H, d, J7Hz, CHCH_3), 2.28 (3H, s, NCH_3), 3.09-3.12 (1H, m, NCH), 3.49 (1H, dd, J10, 6Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.65-3.71 (2H, ABq, J14.5Hz, NCH_2Ar), 3.70 (1H, dd, J10, 3Hz, $\text{CHH}'\text{OCH}_2\text{Ar}$), 3.80 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 4.57 (2H, s, OCH_2Ar), 6.98 (1H, s, aryl CH), 7.11 (1H, td, J8, 1.5Hz, aryl CH), 7.13 (1H, s, aryl CH), 7.28 (1H, td, J7.5, 1Hz, aryl CH), 7.50-7.52 (2H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 12.69, 37.49, 56.22 & 56.40 (4 x CH_3), 57.40 (CH), 57.81, 72.61 & 73.43 (3 x CH_2), 113.14 (CH), 113.91 (quaternary), 115.31 (CH), 122.55 (quaternary), 127.47, 128.87 & 128.96 (3 x CH), 131.29 (quaternary), 132.48 (CH), 138.00, 148.27 & 148.52 (3 x quaternary); m/z (ES) 486 (MH^+ , ^{79}Br ^{79}Br , 70%), 488 (MH^+ , ^{79}Br ^{81}Br , 100%), 490 (MH^+ , ^{81}Br ^{81}Br , 75%); HRMS found 486.0300, $\text{C}_{20}\text{H}_{26}\text{Br}_2\text{NO}_3$ (MH^+ , ^{79}Br ^{79}Br) requires 486.0279.

(S)-[1-Benzyl-2-(2-iodo-benzyloxy)-ethyl]-(2-iodo-benzyl)-amine.²⁰ Colorless oil; yield: 91%; R_f 0.46 (SiO_2 ; Hexane: EtOAc; 4:1); δ_{H} (500MHz, CDCl_3) 2.13 (1H, br s, NH), 2.87-2.94 (2H, m, PhCH_2), 3.08-3.16 (1H, m, NCH), 3.54-3.61 (2H, m, $\text{CH}_2\text{OCH}_2\text{Ar}$), 3.87-3.94 (2H, ABq, J14Hz, NCH_2Ar), 4.48-4.53 (2H, ABq, J12.5Hz, OCH_2Ar), 6.95 (1H, td, J7.5, 1.5Hz, aryl CH), 7.01 (1H, td, J7.5, 1.5Hz, aryl CH), 7.19-7.38 (8H, m, aryl CH), 7.48 (1H, dd, J7.5, 1.5Hz, aryl CH), 7.80 (1H, dd, J8, 1Hz, aryl CH), 7.84 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (125MHz, CDCl_3) 38.36, 55.84, 57.94, 72.21, 76.73, 97.74, 99.62, 126.14, 128.04, 128.09, 128.32, 128.55, 128.78, 129.04, 129.26, 129.52, 138.76, 139.00, 139.24, 140.41, 142.26; m/z (ES) 584 (MH^+ , 100%); HRMS found 583.9947, $\text{C}_{23}\text{H}_{24}\text{I}_2\text{NO}$ (MH^+) requires 583.9947.

(S)-[1-Benzyl-2-(2-bromo-benzyloxy)-ethyl]-(2-bromo-benzyl)-amine.²¹ Colorless oil; yield: 95%; R_f 0.21 (SiO_2 ; Hexane: EtOAc; 9:1); ν_{max} (thin film)/ cm^{-1} 3325m br, 3060s, 3025s, 2858s, 1602m, 1568s, 1495s, 1467s, 1439s, 1358s, 1243s, 1205s, 1106s, 1044s, 1026s, 748s, 700s, 660s; δ_{H} (500MHz, CDCl_3) 2.01 (1H, br s, NH), 2.80-2.88 (2H, m, PhCH_2), 3.05-3.10 (1H, m, NCH), 3.48-3.55 (2H, m, $\text{CH}_2\text{OCH}_2\text{Ar}$), 3.88-3.94 (2H, ABq, J14Hz, NCH_2Ar), 4.50-4.56 (2H, ABq, J13Hz, OCH_2Ar), 7.07 (1H, td, J8, 2Hz, aryl CH), 7.13 (1H, td, J7.5, 1.5Hz, aryl CH), 7.16-7.32 (9H, m, aryl CH), 7.47 (1H, td, J8, 1Hz, aryl CH), 7.51 (1H, dd, J8, 1Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 38.75 & 51.75 (2 x CH_2), 58.29 (CH), 72.71 (CH_2), 122.86 & 124.22 (2 x quaternary), 126.46, 127.55, 127.57, 128.64, 128.68, 129.09, 129.31, 129.54, 130.40, 132.67 & 132.92 (11 x CH), 137.84, 139.03 & 139.59 (3 x quaternary); m/z (ES) 488 (MH^+ , ^{79}Br ^{79}Br , 60%), 490 (MH^+ , ^{79}Br ^{81}Br , 100%), 492 (MH^+ , ^{81}Br ^{81}Br , 50%); HRMS found 488.0206, $\text{C}_{23}\text{H}_{24}\text{Br}_2\text{NO}$ (MH^+ , ^{79}Br ^{79}Br) requires 488.0224.

Biaryl Synthesis.

(1) Method A. An oven-dried, three-necked round-bottomed flask containing the cyclization precursor and equipped with a magnetic stirring bar, a septum, a low temperature thermometer and a vacuum/gas inlet (greased joints) was evacuated and twice heated with a heat gun over 30 minutes. The flask was filled with argon and charged with anhydrous 2-methyltetrahydrofuran (2-MeTHF, 0.05-0.15M). The solution was

(20) The secondary amine of (S)-2-(2-iodobenzylamino)-3-phenyl-propan-1-ol (**1a**) is hindered sterically, sufficient enough to allow a selective alkylation of the alcohol by 2-iodobenzyl chloride.

(21) The secondary amine of (S)-[1-benzyl-2-(2-bromo-benzyloxy)-ethyl]-(2-bromo-benzyl)-amine is hindered sterically, such that (S)-2-amino-3-phenyl-propan-1-ol was only alkylated twice by 2-bromobenzyl bromide.

cooled to -78°C and *t*-BuLi (4.0 equiv.)²² was added dropwise. After addition the reaction was stirred for 30 minutes to give a clear yellow solution of the dilithium intermediate.²³ A freshly prepared solution of CuCN·2LiBr (1M) in 2-MeTHF (1.0 equiv.)²⁴ was added dropwise, then the mixture was stirred for 2 hours allowing the reaction temperature to slowly rise to -40°C . At this temperature a freshly prepared solution of 1,3-dinitrobenzene (1M) in 2-MeTHF (4.0 equiv.)²⁵ was added to give a dark brown-black solution. The solution was allowed to warm to room temperature over 1-12 hours. The black solution was quenched with a 1M solution of HCl in MeOH to give a clear yellow-brown solution and was stirred for 30 minutes. A solution of 10% NH_4OH in saturated aqueous NH_4Cl was added and the resulting two-phase mixture was stirred for 30 minutes, then separated and the aqueous phase was extracted three times with Et_2O . The combined organic layers were washed (saturated aqueous NaCl), dried (K_2CO_3), filtered, concentrated *in vacuo* and chromatographed. In order to determine the thermodynamic diastereomeric ratio (dr) each diastereomer was heated neat under argon at 150°C for 24-48 hours; if the atropisomers were not separable then the mixture was heated until no change in ratio was observed.

(P,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4a. Colorless oil; yield: 88%; kinetic dr: 20:1 (*P:M*); R_f 0.30 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); $[\alpha]_D -13.8$ ($c=1.49$, CH_2Cl_2); ν_{max} (thin film)/ cm^{-1} 2922s, 2854s, 1475s, 1451s, 1094s, 1070s, 755s, 699s; δ_{H} (500MHz, CDCl_3) 2.32 (1H, dd, *J*13.5, 7.5Hz, PhCHH'), 2.38 (3H, s, NCH_3), 2.39-2.44 (1H, m, C(3)H), 2.57 (1H, dd, *J*13.5, 6.5Hz, PhCHH'), 3.22 (1H, dd, *J*12.5, 3.5Hz, C(2)H), 3.39 (1H, dd, *J*12.5, 10Hz, C(2)H), 3.64 (1H, d, *J*14.5Hz, C(5)H), 3.88 (1H, d, *J*14.5Hz, C(5)H), 4.10 (1H, d, *J*12.5Hz, C(10)H), 4.65 (1H, d, *J*12.5Hz, C(10)H), 6.96 (1H, d, *J*7.5Hz, aryl CH), 7.17-7.44 (12H, m, aryl CH); δ_{C} (125MHz, CDCl_3) 35.09 (CH_3), 37.77 (PhCH_2), 59.11 (C5), 64.71 (C3), 72.23 (C2), 73.65 (C10), 125.74, 126.42, 126.71, 127.33, 127.91, 128.04, 128.61, 128.91, 129.27, 129.65 & 130.58 (11 x CH), 138.32, 138.43, 140.03, 141.22 & 143.03 (5 x quaternary); *m/z* (ES) 344 (MH^+ , 100%); HRMS found 344.2004, $\text{C}_{24}\text{H}_{26}\text{NO}$ (MH^+) requires 344.2014.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4a. Colorless crystals; thermodynamic dr: 1:6 (*P:M*); m.p. $134-135^{\circ}\text{C}$ (MeOH); R_f 0.27 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); $[\alpha]_D -37.1$ ($c=0.75$, CH_2Cl_2); ν_{max} (KBr disc)/ cm^{-1} 2943s, 2860s, 1444m, 1088s, 1063s, 757s, 700s; δ_{H} (500MHz, CDCl_3) 2.43 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.55 (3H, s, NCH_3), 2.69-2.74 (1H, m, PhCHH'), 3.37 (1H, dd, *J*12.5, 3.5Hz, C(2)H), 3.43 (1H, br s, C(3)H), 3.59 (1H, d, *J*12Hz, C(5)H), 3.97 (1H, t, *J*11.5Hz, C(2)H), 4.12 (1H, d, *J*12.5Hz, C(5)H), 4.27

(1H, d, *J*9.5Hz, C(10)H), 4.36 (1H, d, *J*9.5Hz, C(10)H), 7.11-7.16 (4H, m, aryl CH), 7.22-7.37 (6H, m, aryl CH), 7.431-7.46 (2H, m, aryl CH), 7.51 (1H, d, *J*7Hz, aryl CH); δ_{C} (125MHz, CDCl_3) 35.46 (CH_3), 35.78 (PhCH_2), 53.89 (C3), 57.15 (C5), 68.23 (C10), 68.53 (C2), 125.91, 126.64, 127.62, 127.78, 128.04, 128.32, 129.34, 130.14, 130.24, 130.41 & 130.66 (11 x CH), 135.13, 138.48, 140.09, 141.00 & 142.04 (5 x quaternary); *m/z* (ES) 344 (MH^+ , 100%). Found: C, 83.7; H, 7.60; N, 4.3%. $\text{C}_{24}\text{H}_{25}\text{NO}$ requires C, 83.9; H, 7.35; N, 4.1%.

(P,10S)-10-Benzyl-16-fluoro-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4b. Colorless oil; yield: 84%; kinetic dr: 13:1 (*P:M*); R_f 0.35 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); ν_{max} (thin film)/ cm^{-1} 2923s, 2856s, 1613s, 1584s, 1478s, 1453s, 1293m, 1195s, 1177s, 1103s, 898m, 751s, 699s; δ_{H} (500MHz, CDCl_3) 2.27 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 2.31 (3H, s, NCH_3), 2.37-2.43 (1H, m, C(3)H), 2.56 (1H, dd, *J*13.5, 6.5Hz, PhCHH'), 3.17 (1H, dd, *J*12.5, 4Hz, C(2)H), 3.26 (1H, dd, *J*12.5, 10Hz, C(2)H), 3.59 (1H, d, *J*14.5Hz, C(5)H), 3.82 (1H, d, *J*14.5Hz, C(5)H), 4.05 (1H, d, *J*12.5Hz, C(10)H), 4.46 (1H, d, *J*12.5Hz, C(10)H), 6.90-6.94 (3H, m, aryl CH), 7.01 (1H, td, *J*9, 3Hz, aryl CH), 7.08 (1H, dd, *J*7.5, 1.5Hz, aryl CH), 7.12-7.17 (2H, m, aryl CH), 7.22 (2H, t, *J*7.5Hz, aryl CH), 7.27 (1H, td, *J*7.5, 1.5Hz, aryl CH), 7.30-7.35 (2H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 36.45 (CH_3), 37.94 (PhCH_2), 59.02 (C5), 65.45 (C3), 72.49 & 73.05 (C2 & C10), 113.96 (d, *J*20.5Hz, CH), 116.91 (d, *J*21.5Hz, CH), 126.00, 126.67, 127.32, 128.28, 128.61, 129.06 & 130.69 (7 x CH), 130.89 (d, *J*8.5Hz, CH), 134.56 (d, *J*3Hz, quaternary), 138.57 & 140.04 (2 x quaternary), 145.21 (d, *J*8.5Hz, quaternary), 162.17 (d, *J*247Hz, quaternary); δ_{F} (282MHz, CDCl_3) -115.80; *m/z* (ES) 344 (MH^+ , 100%); HRMS found 362.1908, $\text{C}_{24}\text{H}_{25}\text{FNO}$ (MH^+) requires 362.1920.

(M,10S)-10-Benzyl-16-fluoro-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4b. Colorless crystals; thermodynamic dr: 1:10 (*P:M*); m.p. $106-108^{\circ}\text{C}$ (EtOH); R_f 0.20 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 97:2:1); ν_{max} (KBr disc)/ cm^{-1} 2923m, 2856m, 1612m, 1584s, 1478s, 1293m, 1177s, 1103s, 898m, 751s, 699s; δ_{H} (500MHz, CDCl_3) 2.33 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.46 (3H, s, NCH_3), 2.62 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 3.25-3.32 (2H, m, C(2)H & C(3)H), 3.50 (1H, d, *J*12.5Hz, C(5)H), 3.86 (1H, dd, *J*12, 10.5Hz, C(2)H), 3.99 (1H, d, *J*12.5Hz, C(5)H), 4.10 (1H, d, *J*10Hz, C(10)H), 4.24 (1H, d, *J*10Hz, C(10)H), 6.86 (1H, dd, *J*9.5, 3Hz, aryl CH), 6.98 (1H, d, *J*8Hz, aryl CH), 7.03-7.07 (4H, m, aryl CH), 7.17 (1H, td, *J*7.5, 1.5Hz, aryl CH), 7.20-7.29 (4H, m, aryl CH), 7.38 (1H, dd, *J*9, 6.5Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 35.70 (CH_3), 36.03 (PhCH_2), 54.04 (C3), 57.37 (C5), 67.60 & 68.74 (C2 & C10), 114.67 (d, *J*20.5Hz, CH), 117.54 (d, *J*21.5Hz, CH), 126.04, 126.84, 128.09, 128.14, 129.43, 130.06 & 130.32 (7 x CH), 131.34 (d, *J*3Hz, quaternary), 132.16 (d, *J*8.5Hz, CH), 137.44, 139.92 & 140.08 (3 x quaternary), 114.24 (d, *J*7.5Hz, quaternary), 162.33 (d, *J*247Hz, quaternary); δ_{F} (282MHz, CDCl_3) -115.29; *m/z* (ES) 344 (MH^+ , 100%); HRMS found 362.1935, $\text{C}_{24}\text{H}_{25}\text{FNO}$ (MH^+) requires 362.1920.

(P,10S)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (P)-4c. Colorless oil; yield: 97%; kinetic dr: 3:1 (*P:M*); R_f 0.22 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 77:20:3); ν_{max} (thin film)/ cm^{-1} 2935s, 2845s, 1600m, 1516s, 1488s, 1445s, 1259s, 1213s, 1141s, 1046s, 1025s, 732s, 700s; δ_{H} (500MHz, CDCl_3) 2.41 (3H, s, NCH_3), 2.52 (1H, dd, *J*13.5, 7.5Hz, PhCHH'), 2.69 (1H, dd, *J*14, 7.5Hz, PhCHH'), 3.18-3.23 (1H, m, C(3)H), 3.36 (1H, d, *J*14Hz, C(5)H),

(22) If more than four equivalents of *t*-BuLi were added, then Ar-*t*-Bu adducts were formed.

(23) The dilithium intermediate could be quenched at this stage by the addition of MeOH (5.0 equiv.). **(1S,2R)-Benzyl-(2-benzoyloxy-1-methyl-2-phenylethyl)-methylamine; 5m.** Colorless oil; yield: 95%; R_f 0.36 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 98:1:1); ν_{max} (thin film)/ cm^{-1} 3084m, 3062s, 3028s, 2966s, 2933s, 2866s, 2791s, 1602m, 1494s, 1453s, 1366s, 1349s, 1068s, 1028s, 759s, 735s, 699s; δ_{H} (500MHz, CDCl_3) 0.92 (3H, d, *J*7Hz, CH_3), 2.39 (3H, s, NCH_3), 3.21 (1H, dq, *J*5.5, 5.5Hz, NCH), 3.76-3.92 (2H, ABq, *J*13.5Hz, NCH_2Ar), 4.34 (1H, d, *J*12Hz, $\text{CHH}'\text{OBn}$), 4.44 (1H, d, *J*8Hz, PhCHH'), 4.54 (1H, d, *J*12Hz, $\text{CHH}'\text{OBn}$), 7.26-7.45 (15H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 13.32 & 37.89 (2 x CH_3), 59.22 (CH_2), 63.23 (CH), 70.76 (CH_2), 84.72, 126.83, 127.71, 127.93, 128.19, 128.27, 128.38, 128.52, 128.59 & 128.92 (10 x CH), 138.99, 141.15 & 141.39 (3 x quaternary); *m/z* (ES) 346 (MH^+ , 100%); HRMS found 346.2186, $\text{C}_{24}\text{H}_{28}\text{NO}$ (MH^+) requires 346.2171. Found: C, 83.4; H, 7.85; N, 4.1%. $\text{C}_{24}\text{H}_{27}\text{NO}$ requires C, 83.4; H, 7.90; N, 4.1%.

(24) Two equivalents of CuCN can be used without effecting the reaction yield or selectivity.

(25) One equivalent of 1,3-dinitrobenzene could be used, but the reaction was less clean and the yield of product lower. Separation of the biaryls from the dinitrobenzene was usually not an issue; however, when it was, then chromatographic differentiation could be attained with a non-base-washed SiO_2 column vs. a base-washed SiO_2 column. Alternatively, an acid/base extraction technique could be employed.

3.85 (1H, d, J 14Hz, C(5)H), 3.86 (3H, s, OCH₃), 3.90 (3H, s, OCH₃), 4.03 (1H, dd, J 11.5, 9.5Hz, C(2)H), 4.14 (1H, dd, J 11.5, 2.5Hz, C(2)H), 6.74 (1H, s, aryl CH), 6.90 (1H, s, aryl CH), 6.99 (1H, d, J 8.5Hz, aryl CH), 7.08-7.31 (8H, m, aryl CH); δ_c (100MHz, CDCl₃) 35.21 (NCH₃), 37.53 (PhCH₂), 56.18 & 56.40 (OCH₃), 60.26 (C5), 65.72 (C3), 69.76 (C2), 112.95, 114.99, 118.17, 123.06, 126.11, 128.38, 128.96 & 129.08 (8 x CH), 129.92 (quaternary), 130.58 (CH), 131.72, 134.45, 140.19, 147.44, 148.09 & 155.96 (6 x quaternary); m/z (ES) 390 (MH⁺, 100%); HRMS found 390.2080, C₂₅H₂₈NO₃ (MH⁺) requires 390.2069.

(M,10S)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4c. Colorless oil; R_f 0.22 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 77:20:3); δ_H (500MHz, CDCl₃) 2.11 (3H, s, NCH₃), 2.58 (1H, dd, J 14, 7.5Hz, PhCHH'), 2.75 (1H, dd, J 14, 9.5Hz, PhCHH'), 3.09 (1H, d, J 13Hz, C(5)H), 3.41-3.44 (1H, m, C(3)H), 3.42 (1H, d, J 13Hz, C(5)H), 3.86 (3H, s, OCH₃), 3.91 (3H, s, OCH₃), 3.95-4.05 (2H, m, C(2)H), 6.73 (1H, s, aryl CH), 6.81 (1H, s, aryl CH), 6.98 (1H, d, J 8.5Hz, aryl CH), 7.08-7.31 (8H, m, aryl CH); δ_c (100MHz, CDCl₃) 36.02 (NCH₃), 36.59 (PhCH₂), 56.18 & 56.35 (OCH₃), 58.37 (C5), 61.71 (C3), 72.84 (C2), 112.58, 112.62, 120.20, 123.17, 126.33, 128.45, 129.08, 129.14 & 129.44 (9 x CH), 130.58, 132.40, 135.47, 139.72, 147.92, 148.09 & 158.80 (7 x quaternary); m/z (ES) 390 (MH⁺, 100%); HRMS found 390.2080, C₂₅H₂₈NO₃ (MH⁺) requires 390.2069.

(P,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[13.4.0.0^{2,7}]nonadeca-1(15),2,4,6,16,18-hexaene; (P)-4d. Colorless oil; yield: 85%; kinetic dr: 1.3:1 ($P:M$); R_f 0.29 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); ν_{max} (thin film)/cm⁻¹ 2923s, 2856s, 1495s, 1473s, 1118s, 748s, 699s; δ_H (500MHz, CDCl₃) 2.38-2.45 (2H, m, PhCHH' and C(10)H), 2.48 (3H, s, NCH₃), 2.56-2.60 (1H, m, C(3)H), 2.82-2.90 (2H, m, PhCHH' and C(10)H), 3.01 (1H, dd, J 10, 2Hz, C(2)H), 3.07 (1H, dd, J 10, 8Hz, C(2)H), 3.31 (1H, d, J 15Hz, C(5)H), 3.37 (1H, dt, J 7, 4Hz, C(11)H), 3.73 (1H, td, J 11, 3Hz, C(11)H), 3.94 (1H, d, J 15Hz, C(5)H), 7.01-7.05 (2H, m, aryl CH), 7.10 (2H, d, J 8Hz, aryl CH), 7.15-7.34 (8H, m, aryl CH), 7.68 (1H, d, J 8Hz, aryl CH); δ_c (125MHz, CDCl₃) 32.68 (PhCH₂), 38.77 (C10), 43.99 (CH₃), 56.90 (C5), 68.14 (C3), 69.62 (C2), 71.76 (C11), 125.52, 125.56, 126.07, 126.93, 127.54, 128.34, 129.22, 129.49, 129.53, 129.63 & 129.95 (11 x CH), 138.41, 139.99, 140.43, 140.90 & 142.21 (5 x quaternary); m/z (ES) 358 (MH⁺, 100%); HRMS found 358.2166, C₂₅H₂₈NO (MH⁺) requires 358.2171.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatricyclo[13.4.0.0^{2,7}]nonadeca-1(15),2,4,6,16,18-hexaene; (M)-4d. Colorless oil; thermodynamic dr: 1:4 ($P:M$); R_f 0.22 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); ν_{max} (thin film)/cm⁻¹ 2926s, 2854s, 1474, 1371m, 1132s, 1030m, 755s, 699s; δ_H (500MHz, CDCl₃) 2.18 (3H, s, NCH₃), 2.31 (1H, dd, J 13.5, 8.5Hz, PhCHH'), 2.59 (1H, ddd, J 14.5, 7.5, 4Hz, C(10)H), 2.72 (1H, dd, J 13.5, 6.5Hz, PhCHH'), 2.87 (1H, ddd, J 14.5, 7.5, 4Hz, C(10)H), 3.00 (1H, dd, J 11.5, 3.5Hz, C(2)H), 3.12-3.14 (1H, m, C(3)H), 3.16 (1H, ddd, J 11, 7.5, 4Hz, C(11)H), 3.39 (1H, dd, J 11, 7.5, 4Hz, C(11)H), 3.44 (1H, d, J 13.5Hz, C(5)H), 3.57 (1H, dd, J 11.5, 10Hz, C(2)H), 3.77 (1H, d, J 13.5Hz, C(5)H), 7.02 (1H, d, J 7.5Hz, aryl CH), 7.08-7.10 (2H, m, aryl CH), 7.18-7.30 (10H, m, aryl CH); δ_c (125MHz, CDCl₃) 35.18 (PhCH₂), 35.53 (C10), 36.52 (CH₃), 57.13 (C5), 57.34 (C3), 69.75 (C2 & C11), 125.65, 126.05, 126.27, 126.96, 127.25, 128.40, 129.12, 129.28, 129.40, 129.59 & 130.22 (11 x CH), 137.59, 138.39, 140.30, 141.68 & 142.36 (5 x quaternary); m/z

(ES) 358 (MH⁺, 100%); HRMS found 358.2173, C₂₅H₂₈NO (MH⁺) requires 358.2171.

(P,10S)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4e. Colorless crystals; yield: 92%; kinetic dr: 16:1 ($P:M$); m.p. 143-144°C (MeOH); R_f 0.18 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 88:10:2); $[\alpha]_D$ +1.93 (c=1.50, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 2986s, 2919s, 1604m, 1509s, 1438s, 1245s, 1101s, 951s, 865s, 758s, 699s; δ_H (500MHz, CDCl₃) 2.33 (1H, dd, J 13, 8.5Hz, PhCHH'), 2.40 (3H, s, NCH₃), 2.40-2.45 (1H, m, C(3)H), 2.60 (1H, dd, J 13, 5.5Hz, PhCHH'), 3.26-3.35 (2H, m, C(2)H), 3.51 (1H, d, J 14.5Hz, C(5)H), 3.85 (1H, d, J 14.5Hz, C(5)H), 3.84 (3H, s, OCH₃), 3.96 (3H, s, OCH₃), 4.15 (1H, d, J 12Hz, C(10)H), 4.51 (1H, d, J 12Hz, C(10)H), 6.65 (1H, s, aryl CH), 6.96-6.97 (3H, m, aryl CH), 7.17-7.28 (5H, m, aryl CH), 7.35-7.42 (2H, m, aryl CH); δ_c (125MHz, CDCl₃) 36.91 (NCH₃), 37.96 (PhCH₂), 55.80 & 55.82 (OCH₃), 58.32 (C5), 64.78 (C3), 72.27 (C2), 73.42 (C10), 111.81, 113.28, 125.67, 127.27, 127.88, 127.96, 128.83, 129.21 & 130.02 (9 x CH), 131.29, 132.73, 138.31, 139.81, 142.65, 146.84 & 147.30 (7 x quaternary); m/z (ES) 404 (MH⁺, 100%). Found: C, 77.0; H, 7.05; N, 3.4%. C₂₆H₂₉NO₃ requires C, 77.4; H, 7.25; N, 3.5%.

(M,10S)-10-Benzyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4e. Colorless crystals; thermodynamic dr: 1:11 ($P:M$); m.p. 146-148°C (MeOH); R_f 0.26 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 87:10:3); $[\alpha]_D$ +10.4 (c=1.08, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 2936s, 2848s, 1512s, 1243s, 1206s, 1143s, 1090s, 755s, 699s; δ_H (500MHz, CDCl₃) 2.36 (1H, dd, J 13.5, 6Hz, PhCHH'), 2.51 (3H, s, NCH₃), 2.68 (1H, dd, J 13.5, 9Hz, PhCHH'), 3.30 (1H, dd, J 12, 4Hz, C(2)H), 3.43-3.48 (1H, m, C(3)H), 3.52 (1H, d, J 12Hz, C(5)H), 3.56 (3H, s, OCH₃), 3.83 (3H, s, OCH₃), 3.92 (1H, t, J 11.5Hz, C(2)H), 4.01 (1H, d, J 12Hz, C(5)H), 4.22 (1H, d, J 9.5Hz, C(10)H), 4.30 (1H, d, J 9.5Hz, C(10)H), 6.56 (1H, s, aryl CH), 6.68 (1H, s, aryl CH), 7.11-7.46 (9H, m, aryl CH); δ_c (100MHz, CDCl₃) 35.18, 35.82, 52.58, 55.71, 55.75, 57.24, 68.04, 68.66, 111.58, 112.51, 125.65, 127.49, 127.92, 128.10, 129.15, 129.36, 130.15, 130.63, 132.61, 134.95, 139.79, 141.55, 146.96, 148.26; m/z (ES) 404 (MH⁺, 100%). Found: C, 77.2; H, 7.35; N, 3.4%. C₂₆H₂₉NO₃ requires C, 77.4; H, 7.25; N, 3.5%.

(P,10S)-10-Benzyl-9-methyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-1(14),2,4,6,15,17(22),18,20-octane; (P)-4f. Colorless crystals; yield: 92%; kinetic dr: 1.5:1 ($P:M$); m.p. 142-144°C (*i*-PrOH); R_f 0.36 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (KBr disc)/cm⁻¹ 2940s, 2866s, 1449s, 1340s, 1103s, 1090s, 1056s, 826s, 759s, 638s; δ_H (500MHz, CDCl₃) 2.25 (1H, dd, J 13.5, 8.5Hz, PhCHH'), 2.27 (3H, s, NCH₃), 2.33-2.39 (1H, m, C(3)H), 2.46 (1H, dd, J 13.5, 6Hz, PhCHH'), 3.21 (1H, dd, J 12.5, 4Hz, C(2)H), 3.35 (1H, dd, J 12.5, 10Hz, C(2)H), 3.42 (1H, d, J 15Hz, C(5)H), 3.56 (1H, d, J 15Hz, C(5)H), 4.19 (1H, d, J 12.5Hz, C(10)H), 4.69 (1H, d, J 12.5Hz, C(10)H), 6.82 (2H, d, J 7.5Hz, aryl CH), 7.09-7.16 (4H, m, aryl CH), 7.28-7.41 (6H, m, aryl CH), 7.46 (1H, t, J 7.5Hz, aryl CH), 7.85 (1H, d, J 8.5Hz, aryl CH), 7.90 (1H, d, J 8Hz, aryl CH); δ_c (100MHz, CDCl₃) 35.72 (CH₃), 38.22 (PhCH₂), 59.72 (C5), 64.96 (C3), 72.99 & 74.35 (C2 & C10), 125.93, 126.10, 126.27, 126.58, 127.22, 127.63, 127.74, 128.16, 128.24, 129.04, 129.55 & 130.89 (12 x CH), 132.83, 133.29, 135.89, 138.82, 139.74, 140.02 & 140.22 (7 x quaternary); m/z (ES) 394 (MH⁺, 100%). Found: C, 85.7; H, 7.05; N, 3.5%. C₂₈H₂₇NO requires C, 85.5; H, 6.90; N, 3.6%.

(M,10S)-10-Benzyl-9-methyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-

1(14),2,4,6,15,17(22),18,20-octaene; (M)-4f. Colorless oil; thermodynamic dr: 1:2 (*P:M*); R_f 0.32 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); $\nu_{\max}$ (thin film)/cm⁻¹ 2929s, 2853s, 1495s, 1454s, 1383s, 1088s, 1064s, 909s, 822s, 733s, 698s; δ_H (500MHz, CDCl₃) 2.32 (3H, s, NCH₃), 2.41 (1H, dd, *J*13.5, 5.5Hz, PhCHH'), 2.64 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 3.20-3.23 (1H, m, C(3)H), 3.23 (1H, dd, *J*13.5, 9Hz, C(2)H), 3.44 (1H, d, *J*12Hz, C(5)H), 3.67 (1H, d, *J*12Hz, C(5)H), 3.71 (1H, dd, *J*13.5, 4Hz, C(2)H), 4.35 (1H, d, *J*10.5Hz, C(10)H), 4.46 (1H, d, *J*10.5Hz, C(10)H), 7.02-7.07 (2H, m, aryl CH), 7.15 (1H, dd, *J*7, 2Hz, aryl CH), 7.21-7.33 (8H, m, aryl CH), 7.45 (1H, td, *J*6.5, 1Hz, aryl CH), 7.57 (1H, d, *J*8.5Hz, aryl CH), 7.86 (1H, d, *J*8.5Hz, aryl CH), 7.89 (1H, d, *J*8.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 36.03 (CH₃), 36.45 (PhCH₂), 54.34 (C3), 56.77 (C5), 67.04 & 68.38 (C2 & C10), 125.98, 126.02, 126.14, 126.69, 127.19, 127.86, 127.95, 128.03, 128.14, 128.26, 129.33, 130.85 & 131.18 (13 x CH), 132.59, 133.49, 138.26, 138.32, 138.90 & 140.20 (6 x quaternary); *m/z* (ES) 394 (MH⁺, 100%). Found: C, 85.6; H, 6.85; N, 3.7%. C₂₈H₂₇NO requires C, 85.5; H, 6.90; N, 3.6%.

(S)-10-Benzyl-11-methyl-8-oxa-4-thia-11-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,5,14,16-pentaene; 4g. Colorless crystals; yield: 86%; m.p. 151-152°C (MeOH); R_f 0.14 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); $\nu_{\max}$ (KBr disc)/cm⁻¹ 2940s, 2860s, 1450s, 1090s, 1064s, 802s, 765s; δ_H (500MHz, CDCl₃) 2.31 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.49 (3H, s, NCH₃), 2.60 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 3.27 (1H, dd, *J*12.5, 3.5Hz, C(2)H), 3.30-3.34 (1H, m, C(3)H), 3.47 (1H, d, *J*12.5Hz, C(5)H), 3.91 (1H, dd, *J*12.5, 10.5Hz, C(2)H), 3.99 (1H, d, *J*10.5Hz, C(10)H), 4.11 (1H, d, *J*12.5Hz, C(5)H), 4.37 (1H, d, *J*10.5Hz, C(10)H), 6.95 (1H, d, *J*8Hz, aryl CH), 7.01-7.04 (3H, m, aryl CH), 7.09-7.27 (6H, m, aryl CH), 7.36 (1H, d, *J*3.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 35.90 (CH₃), 35.94 (PhCH₂), 54.42 (C3), 57.53, 63.58 & 69.36 (C2, C5 & C10), 124.04, 125.99, 126.02, 126.67, 128.16, 128.17, 129.50, 130.39 & 131.19 (9 x CH), 136.53, 137.63, 138.44, 140.14 & 143.18 (5 x quaternary); *m/z* (ES) 344 (MH⁺, 100%). Found: C, 75.9; H, 6.70; N, 4.0; S, 9.5%. C₂₂H₂₃NOS requires C, 75.6; H, 6.65; N, 4.0; S, 9.2%.

(S)-10-Benzyl-17-chloro-9-methyl-12-oxa-21-thia-9-azatetracyclo[12.7.0.0^{2,7}.0^{15,20}]uncosa-1(14),2,4,6,15,17,19-heptaene; 4h. Colorless crystals; yield: 73%; m.p. 126-128°C (*i*-PrOH); R_f 0.31 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); $\nu_{\max}$ (KBr disc)/cm⁻¹ 2926s, 2854s, 1584m, 1438s, 1421s, 1114s, 1078s, 1039s, 744s, 699s; δ_H (500MHz, CDCl₃, 40°C) 2.25 (1H, dd, *J*13.5, 7.5Hz, PhCHH'), 2.48 (3H, s, NCH₃), 2.77 (1H, dd, *J*13.5, 6Hz, PhCHH'), 3.25 (1H, d, *J*12.5Hz, C(5)H), 3.28-3.31 (2H, m, C(2)H & C(3)H), 3.64 (1H, dd, *J*13.5, 11Hz, C(2)H), 4.05 (1H, d, *J*12.5Hz, C(5)H), 4.69 (1H, d, *J*11.5Hz, C(10)H), 4.96 (1H, br d, *J*11.5Hz, C(10)H), 7.04 (2H, d, *J*7.5Hz, aryl CH), 7.14-7.34 (8H, m, aryl CH), 7.73 (1H, d, *J*8.5Hz, aryl CH), 7.92 (1H, d, *J*2Hz, aryl CH); δ_C (100MHz, CDCl₃) 33.91, 38.12, 54.39, 61.28, 62.80, 65.19, 122.78, 123.13, 125.26, 126.11, 127.06, 128.43, 128.95, 129.31, 129.71, 131.25, 131.49, 131.91, 133.19, 137.69, 138.07, 140.07, 141.08, 144.47; *m/z* (ES) 434 (MH⁺, ³⁵Cl, 100%), 436 (MH⁺, ³⁷Cl, 36%); HRMS found 434.1349, C₂₆H₂₅ClNOS (MH⁺) requires 434.1345.

(S)-11-Benzyl-12-methyl-9-oxa-3,12-diazatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; 4i. Colorless oil; yield: 70%; R_f 0.26 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 77:20:3); $\nu_{\max}$ (thin film)/cm⁻¹ 2931s, 2853s, 1567s, 1431s, 1088s, 1062s,

759s, 699s; δ_H (500MHz, CDCl₃) 2.33 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.42 (3H, s, NCH₃), 2.65 (1H, dd, *J*13.5, 8.5Hz, PhCHH'), 3.29-3.34 (2H, m, C(2)H & C(3)H), 3.54 (1H, d, *J*12.5Hz, C(5)H), 3.84 (1H, td, *J*12, 2Hz, C(2)H), 3.95 (1H, d, *J*12.5Hz, C(5)H), 4.24-4.30 (2H, ABq, *J*10.5Hz, C(10)H), 7.00 (1H, d, *J*8Hz, aryl CH), 7.05 (2H, d, *J*8.5Hz, aryl CH), 7.16-7.31 (7H, m, aryl CH), 7.73 (1H, dd, *J*8, 2Hz, aryl CH), 8.63 (1H, dd, *J*5, 2Hz, aryl CH); δ_C (100MHz, CDCl₃) 35.67 (CH₃), 35.73 (PhCH₂), 54.67 (C3), 57.27, 67.85 & 69.01 (C2, C5 & C10), 122.69, 126.08, 127.12, 128.18, 128.41, 129.40, 129.67 & 130.18 (8 x CH), 131.26 & 136.97 (2 x quaternary), 138.25 (CH), 139.98 & 140.20 (2 x quaternary), 149.34 (CH), 159.86 (quaternary); *m/z* (ES) 345 (MH⁺, 100%); HRMS found 345.1970, C₂₃H₂₅N₂O (MH⁺) requires 345.1967.

(P,10S)-9,10-Dibenzyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4j. Colorless oil; yield: 94%; kinetic dr: 2.2:1 (*P:M*); R_f 0.18 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); $\nu_{\max}$ (thin film)/cm⁻¹ 3059m, 3024s, 2920s, 2855s, 1601m, 1494s, 1475m, 1452s, 1367m, 1342m, 1199m, 1091s, 1028m, 1007m, 984m, 947m, 755s, 730s, 698s; δ_H (500MHz, CDCl₃) 2.33-2.39 (1H, m, PhCHH'), 2.60-2.67 (2H, m, C(3)H and PhCHH'), 3.25 (1H, dd, *J*12.5, 4Hz, C(2)H), 3.34 (1H, dd, *J*12.5, 9.5Hz, C(2)H), 3.56 (1H, d, *J*15Hz, C(5)H), 3.71 (2H, s, PhCH₂N), 3.73 (1H, d, *J*15Hz, C(5)H), 4.12 (1H, d, *J*12Hz, C(10)H), 4.58 (1H, d, *J*12Hz, C(10)H), 6.90 (2H, d, *J*7Hz, aryl CH), 7.08-7.42 (16H, m, aryl CH); δ_C (100MHz, CDCl₃) 39.03, 51.33, 53.97, 64.95, 72.84, 73.96, 125.99, 126.50, 126.82, 126.92, 127.54, 128.19, 128.28, 128.45, 128.57, 128.88, 129.12, 129.76, 129.87, 130.73, 138.22, 138.61, 140.10, 140.56, 141.44, 143.34; *m/z* (ES) 420 (MH⁺, 100%); HRMS found 420.2345, C₃₀H₃₀NO (MH⁺) requires 420.2327.

(M,10S)-9,10-Dibenzyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4j. Colorless oil; thermodynamic dr: 1:7 (*P:M*); R_f 0.16 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); $\nu_{\max}$ (thin film)/cm⁻¹ 3060s, 3024s, 2943s, 2856s, 1601m, 1494s, 1452s, 1388m, 1363m, 1224m, 1128m, 1100s, 1086s, 1061s, 909m, 757s, 729s, 697s; δ_H (500MHz, CDCl₃) 2.52 (1H, dd, *J*13.5, 6Hz, PhCHH'), 2.72 (1H, dd, *J*13.5, 9Hz, PhCHH'), 3.41 (1H, d, *J*12.5Hz, C(5)H), 3.43 (1H, dd, *J*12.5, 3.5Hz, C(2)H), 3.56 (1H, d, *J*14Hz, NCHH'Ph), 3.62-3.68 (1H, m, C(3)H), 3.88 (1H, d, *J*12.5Hz, C(5)H), 3.99 (1H, dd, *J*12.5, 10.5Hz, C(2)H), 4.22 (1H, d, *J*14Hz, NCHH'Ph), 4.23 (1H, d, *J*9.5Hz, C(10)H), 4.34 (1H, d, *J*9.5Hz, C(10)H), 7.05-7.46 (18H, m, aryl CH); δ_C (100MHz, CDCl₃) 36.70, 51.65 & 53.31 (3 x CH₂), 53.43 (CH), 68.41 & 70.26 (2 x CH₂), 126.25, 126.68, 126.77, 127.78, 127.98, 128.24, 128.34, 128.41, 128.58, 129.74, 130.04, 130.36, 130.61 & 130.98 (14 x CH), 134.93, 137.98, 139.90, 140.47, 141.17 & 142.08 (6 x quaternary); *m/z* (ES) 420 (MH⁺, 100%); HRMS found 420.2319, C₃₀H₃₀NO (MH⁺) requires 420.2327.

(P,10S)-10-Benzyl-9-(2,4,6-trimethoxybenzyl)-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4k. Colorless oil; yield: 88%; kinetic dr: 1.1:1 (*P:M*); R_f 0.12 (SiO₂; Hexane: EtOAc: 4:1); δ_H (500MHz, CDCl₃) 2.37 (1H, dd, *J*13.5, 9Hz, PhCHH'), 2.82-2.87 (1H, m, C(3)H), 2.90 (1H, dd, *J*13.5, 4.5Hz, PhCHH'), 3.00 (1H, dd, *J*11, 8Hz, C(2)H), 3.43 (1H, dd, *J*11, 3Hz, C(2)H), 3.55 (1H, d, *J*13Hz, NCHH'), 3.57 (1H, d, *J*15Hz, C(5)H), 3.75 (6H, s, OCH₃), 3.77 (1H, d, *J*13Hz, NCHH'), 3.80 (3H, s, OCH₃), 3.90 (1H, d, *J*15Hz, C(5)H), 4.16-4.27 (2H, ABq, *J*11.5Hz, C(10)H), 6.11 (2H, s, aryl CH), 6.98-7.34 (12H, m, aryl CH), 7.47 (1H, d, *J*7.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 38.29, 46.45, 52.69, 55.56, 55.75, 64.82, 71.71, 73.32, 90.76, 109.82, 125.53,

(26) At 25°C C(10)H' appears as a broad singlet.

125.61, 127.14, 127.21, 127.86, 128.08, 128.82, 129.34, 129.54, 129.63, 129.86, 137.55, 140.47, 141.01, 143.13, 143.35, 160.04, 160.32; m/z (ES) 510 (MH^+ , 100%). Found: C, 77.8; H, 6.95; N, 2.7%. $C_{33}H_{35}NO_4$ requires C, 77.8; H, 6.90; N, 2.8%.

(M,10S)-10-Benzyl-9-(2,4,6-trimethoxybenzyl)-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4k. Colorless oil; thermodynamic dr: 1:3 (*P:M*); R_f 0.29 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 2934s, 1606s, 1495m, 1454s, 1416m, 1319m, 1226s, 1204s, 1151s, 1119s, 1059m, 951m, 813m, 757s, 700s; δ_H (500MHz, CDCl₃) 2.37 (1H, dd, J13.5, 8.5Hz, PhCHH'), 3.05 (1H, dd, J13.5, 5Hz, PhCHH'), 3.20 (1H, dd, J12.5, 4Hz, C(2)H), 3.30-3.36 (1H, m, C(3)H), 3.46 (1H, d, J12.5Hz, NCHH'), 3.65 (6H, s, OCH₃), 3.77 (1H, d, J12Hz, C(5)H), 3.80 (3H, s, OCH₃), 3.86 (1H, t, J11.5Hz, C(2)H), 3.94 (1H, d, J12Hz, C(5)H), 3.97 (1H, d, J12.5Hz, NCHH'), 4.24 (1H, d, J10.5Hz, C(10)H), 4.45 (1H, d, J10.5Hz, C(10)H), 6.10 (2H, s, aryl CH), 7.04-7.38 (12H, m, aryl CH), 7.44 (1H, dd, J8, 1.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 35.78, 40.13, 53.08, 55.55, 55.64, 56.01, 67.33, 68.16, 90.70, 109.31, 125.67, 126.35, 127.28, 127.73, 128.02, 128.14, 129.29, 130.38, 130.41, 130.48, 130.94, 135.83, 138.68, 141.32, 141.36, 142.56, 160.17, 160.36; m/z (ES) 510 (MH^+ , 100%). Found: C, 77.8; H, 7.00; N, 2.7%. $C_{33}H_{35}NO_4$ requires C, 77.8; H, 6.90; N, 2.8%.

(P,10S,11S)-9,10-Dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4m. Colorless crystals; yield: 88%; kinetic dr: 17:1 (*P:M*); m.p. 97-98°C (MeOH); R_f 0.38 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 98:1:1); $[\alpha]_D$ +25.8 (c=0.66, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 2933s, 1452s, 1071s, 758s, 701s; δ_H (500MHz, CDCl₃) 0.64 (3H, d, J6.5Hz, C(3)CH₃), 2.29 (3H, s, NCH₃), 2.61-2.64 (1H, m, C(3)H), 3.50 (1H, d, J14Hz, C(5)H), 3.53 (1H, d, J9Hz, C(2)H), 3.95 (1H, d, J11.5Hz, C(10)H), 4.06 (1H, d, J14Hz, C(5)H), 4.33 (1H, d, J11.5Hz, C(10)H), 7.05 (2H, d, J7Hz, aryl CH), 7.10 (1H, d, J7.5Hz, aryl CH), 7.22-7.38 (8H, m, aryl CH), 7.44 (1H, t, J7.5Hz, aryl CH), 7.23 (1H, d, J7.5Hz, aryl CH); δ_C (125MHz, CDCl₃) 15.36 (C(3)CH₃), 45.72 (NCH₃), 55.87 (C5), 64.21 (C3), 72.16 (C10), 87.55 (C2), 126.21, 127.23, 127.30, 127.43, 127.44, 127.58, 128.16, 128.76, 129.36, 129.88 & 129.93 (11 x CH), 137.90, 140.90, 140.94, 142.02 & 142.62 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%). Found: C, 83.9; H, 7.40; N, 4.0%. $C_{24}H_{25}NO$ requires C, 83.9; H, 7.35; N, 4.1%.

(M,10S,11S)-9,10-Dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4m. Colorless oil; thermodynamic dr: 1:1.5 (*P:M*); R_f 0.30 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 98:1:1); $[\alpha]_D$ +55.3 (c=0.62, CH₂Cl₂); ν_{max} (thin film)/cm⁻¹ 2928s, 2871s, 2790s, 1451s, 1364s, 1195s, 1084s, 1061s, 754s, 700s; δ_H (500MHz, CDCl₃) 0.67 (3H, d, J6.5Hz, C(3)CH₃), 2.58 (3H, s, NCH₃), 3.20 (1H, d, J13.5Hz, C(5)H), 3.26-3.30 (1H, m, C(3)H), 3.74 (1H, d, J13.5Hz, C(5)H), 4.16 (1H, d, J10Hz, C(2)H), 4.24 (1H, d, J12Hz, C(10)H), 5.09 (1H, d, J12Hz, C(10)H), 7.15-7.21 (2H, m, aryl CH), 7.27-7.44 (10H, m, aryl CH), 7.53 (1H, d, J7.5Hz, aryl CH); δ_C (125MHz, CDCl₃) 10.37 (C(3)CH₃), 40.59 (NCH₃), 52.12 (C5), 61.62 (C3), 68.51 (C10), 78.54 (C2), 126.53, 127.10, 127.39, 127.59, 127.68, 128.06, 128.25, 129.44, 129.76, 129.90 & 130.55 (11 x CH), 136.04, 138.55, 140.49, 140.73 & 142.66 (5 x quaternary); m/z (ES) 344 (MH^+ , 100%). Found: C, 84.0; H, 7.40; N, 4.0%. $C_{24}H_{25}NO$ requires C, 83.9; H, 7.35; N, 4.1%.

(P,10S,11S)-5,16-Dichloro-9,10-dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-

1(14),2,4,6,15,17-hexaene; (P)-4n. Colorless crystals; yield: 94%; kinetic dr: 6:1 (*P:M*); m.p. 169.5-170.5°C (MeOH); R_f 0.56 (base-washed SiO₂; Hexane); $[\alpha]_D$ +99.7 (c=1.70, CH₂Cl₂); ν_{max} (KBr disc)/cm⁻¹ 2910s, 2783s, 2763s, 1589m, 1453s, 1224s, 1096s, 1084s, 821s, 767s, 703s; δ_H (500MHz, CDCl₃) 0.68 (3H, d, J6.5Hz, C(3)CH₃), 2.36 (3H, s, NCH₃), 2.65 (1H, dq, J9.5, 6.5Hz, C(3)H), 3.48 (1H, d, J14.5Hz, C(5)H), 3.61 (1H, d, J9.5Hz, C(2)H), 3.83 (1H, d, J11Hz, C(10)H), 4.09 (1H, J14.5Hz, C(5)H), 4.26 (1H, d, J11Hz, C(10)H), 7.02 (1H, d, J8Hz, aryl CH), 7.12-7.15 (3H, m, aryl CH), 7.29-7.39 (6H, m, aryl CH), 7.82 (1H, d, J2Hz, aryl CH); δ_C (100MHz, CDCl₃) 16.22 (C(3)CH₃), 45.62 (NCH₃), 55.58 (C5), 63.99 (C3), 71.26 (C10), 87.51 (C2), 126.19, 127.02, 127.48, 127.55, 128.12, 129.03, 129.65, 130.12 & 131.06 (9 x CH), 132.95, 133.52, 137.28, 139.29, 139.54, 140.98 & 142.95 (7 x quaternary); m/z (ES) 412 (MH^+ , ³⁵Cl, 100%), 414 (MH^+ , ³⁷Cl, 62%). Found: C, 70.0; H, 5.70; Cl, 17.1; N, 3.4%. $C_{24}H_{23}Cl_2NO$ requires C, 69.9; H, 5.60; Cl, 17.2; N, 3.4%.

(M,10S,11S)-5,16-Dichloro-9,10-dimethyl-11-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4n. Colorless oil; thermodynamic dr: 1:2 (*P:M*); R_f 0.28 (base-washed SiO₂; Hexane); $[\alpha]_D$ +28.5 (c=0.80, CH₂Cl₂); ν_{max} (thin film)/cm⁻¹ 2928s, 2795s, 1591m, 1470s, 1193s, 1099s, 909s, 732s, 701s; δ_H (500MHz, CDCl₃) 0.65 (3H, d, J7Hz, C(3)CH₃), 2.49 (3H, s, NCH₃), 3.17 (1H, d, J14Hz, C(5)H), 3.16-3.19 (1H, m, C(3)H), 3.60 (1H, d, J14Hz, C(5)H), 4.00 (1H, d, J10Hz, C(2)H), 4.07 (1H, d, J12Hz, C(10)H), 4.87 (1H, d, J12Hz, C(10)H), 7.02 (1H, d, J8.5Hz, aryl CH), 7.06 (1H, d, J8.5Hz, aryl CH), 7.25-7.39 (8H, m, aryl CH), 7.49 (1H, d, J2Hz, aryl CH); δ_C (100MHz, CDCl₃) 10.73 (C(3)CH₃), 40.43 (NCH₃), 52.38 (C5), 61.27 (C3), 68.17 (C10), 79.63 (C2), 126.64, 127.74, 127.76, 127.87, 128.30, 129.21, 129.64, 130.46 & 131.42 (9 x CH), 132.95, 133.25, 137.93, 138.00, 139.68, 139.89 & 141.10 (7 x quaternary); m/z (ES) 412 (MH^+ , Cl³⁵, 100%), 414 (MH^+ , Cl³⁷, 60%). Found: C, 70.0; H, 5.75; Cl, 17.1; N, 3.4%. $C_{24}H_{23}Cl_2NO$ requires C, 69.9; H, 5.60; Cl, 17.2; N, 3.4%.

(M,10R)-4,5-Dimethoxy-9-methyl-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4o. Colorless oil; yield: 84%; kinetic dr: 1:23 (*P:M*); R_f 0.18 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 97:2:1); ν_{max} (thin film)/cm⁻¹ 2907s, 2864s, 2788m, 1604m, 1512s, 1243s, 1206s, 1134s, 1102s, 758s, 732s, 702s; δ_H (500MHz, CDCl₃) 2.30 (3H, s, NCH₃), 3.21 (1H, t, J10Hz, C(2)H), 3.36 (1H, d, J14.5Hz, C(5)H), 3.45 (1H, dd, J10, 2Hz, C(3)H), 3.55 (1H, dd, J10, 2Hz, C(2)H), 3.83 (3H, s, OCH₃), 3.86 (1H, d, J10.5Hz, C(10)H), 4.07 (3H, s, OCH₃), 4.19 (1H, d, J14.5Hz, C(5)H), 4.45 (1H, d, J10.5Hz, C(10)H), 7.22 (1H, s, aryl CH), 7.23-7.39 (9H, m, aryl CH), 7.61 (1H, s, aryl CH); δ_C (125MHz, CDCl₃) 46.02 (NCH₃), 55.44 (C5), 56.19 & 56.23 (OCH₃), 70.58 (C3), 73.32 (C2), 76.21 (C10), 112.56, 112.95, 127.35, 127.77, 127.79, 128.41, 128.58, 129.14 & 130.54 (9 x CH), 131.34, 134.16, 137.68, 142.82, 143.28, 146.90 & 148.58 (7 x quaternary); m/z (ES) 390 (MH^+ , 100%); HRMS found 390.2086, $C_{25}H_{28}NO_3$ (MH^+) requires 390.2069.

(P,10R)-4,5-Dimethoxy-9-methyl-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4o. Colorless crystals; thermodynamic dr: 2:1 (*P:M*); m.p. 197-199°C (EtOH); R_f 0.33 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (KBr disc)/cm⁻¹ 2933m, 2846m, 1604m, 1514s, 1241s, 1207s, 1139s, 756s, 733s, 699s; δ_H (500MHz, CDCl₃) 2.32 (3H, s, NCH₃), 3.64 (1H, d, J12Hz, C(5)H), 3.78 (1H, dd, J11.5, 3.5Hz, C(3)H), 3.85 (3H, s, OCH₃), 3.99 (3H, s, OCH₃), 4.12 (1H, d, J12Hz, C(5)H),

4.31 (1H, dd, J 10.5, 3.5Hz, C(2)H), 4.35 (1H, d, J 11.5Hz, C(2)H), 4.37-4.40 (2H, ABq, J 7.5Hz, C(10)H₂), 6.62 (1H, s, aryl CH), 7.22-7.25 (2H, m, aryl CH), 7.29-7.34 (5H, m, aryl CH), 7.38-7.43 (2H, m, aryl CH), 7.48-7.50 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 36.12 (NCH₃), 53.38 (C3), 56.24 & 56.33 (OCH₃), 57.51 (C5), 66.60 & 68.39 (C2 & C10), 111.99, 113.22, 127.00, 127.84, 128.00, 128.34 & 128.55 (7 x CH), 130.29 (quaternary), 130.63 & 131.14 (2 x CH), 133.48, 135.37, 140.82, 142.03, 147.64 & 148.86 (6 x quaternary); m/z (ES) 390 (MH⁺, 100%); HRMS found 390.2055, C₂₅H₂₈NO₃ (MH⁺) requires 390.2069.

(P,10S)-10-tert-Butyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(P)-4p.** Colorless oil; yield: 83%; kinetic dr: 4:1 (*P:M*); R_f 0.30 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (thin film)/cm⁻¹ 2950s, 1515s, 1484s, 1464s, 1337s, 1236s, 1210s, 1109s; δ_H (500MHz, CDCl₃) 0.61 (9H, s, C(CH₃)₃), 1.52 (1H, dd, J 11, 4.5Hz, C(3)H), 2.28 (3H, s, NCH₃), 3.42 (1H, dd, J 13, 4.5Hz, C(2)H), 3.63-3.74 (2H, ABq, J 14Hz, C(5)H₂), 3.70 (1H, dd, J 13, 11Hz, C(2)H), 3.82 (3H, s, OCH₃), 3.92 (3H, s, OCH₃), 4.08 (1H, d, J 12.5Hz, C(10)H), 4.89 (1H, d, J 12.5Hz, C(10)H), 6.69 (1H, s, aryl CH), 6.74 (1H, s, aryl CH), 7.20 (1H, d, J 7.5Hz, aryl CH), 7.31 (1H, t, J 7Hz, aryl CH), 7.34 (1H, d, J 6.5Hz, aryl CH), 7.39 (1H, t, J 7.5Hz, aryl CH); δ_c (100MHz, CDCl₃) 27.26, 34.70, 35.83, 55.76, 55.79, 61.95, 68.38, 69.74, 73.62, 111.44, 114.58, 126.92, 127.73, 129.23, 129.78, 130.21, 133.26, 138.82, 143.47, 146.33, 146.65; m/z (ES) 370 (MH⁺, 100%); HRMS found 370.2390, C₂₃H₃₂NO₃ (MH⁺) requires 370.2382.

(M,10S)-10-tert-Butyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(M)-4p.** Colorless oil; thermodynamic dr: 1:2 (*P:M*); R_f 0.45 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (thin film)/cm⁻¹ 2951s, 2847m, 1605m, 1513s, 1242s, 1207s, 1141s, 1090s, 755m; δ_H (500MHz, CDCl₃) 0.94 (9H, s, C(CH₃)₃), 2.42 (3H, s, NCH₃), 2.83 (1H, dd, J 10.5, 3.5Hz, C(3)H), 3.52 (1H, dd, J 12, 3.5Hz, C(2)H), 3.54 (1H, d, J 12Hz, C(5)H), 3.85 (3H, s, OCH₃), 3.92 (1H, d, J 12Hz, C(5)H), 3.94 (3H, s, OCH₃), 4.07 (1H, dd, J 12, 10.5Hz, C(2)H), 4.19 (1H, d, J 9.5Hz, C(10)H), 4.26 (1H, d, J 9.5Hz, C(10)H), 6.58 (1H, s, aryl CH), 7.15 (1H, s, aryl CH), 7.15-7.17 (1H, m, aryl CH), 7.36-7.38 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 29.25, 33.78, 37.91, 55.67, 55.74, 57.12, 59.60, 65.00, 67.50, 112.52, 112.71, 127.48, 128.05, 130.15, 130.30, 130.89, 133.18, 135.02, 141.70, 147.30, 148.08; m/z (ES) 370 (MH⁺, 100%); HRMS found 370.2389, C₂₃H₃₂NO₃ (MH⁺) requires 370.2382.

(P,10S)-10-Cyclohexylmethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(P)-4q.** Colorless oil; yield: 88%; kinetic dr: 22:1 (*P:M*); R_f 0.28 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (thin film)/cm⁻¹ 2920s, 2848s, 1605m, 1515s, 1485s, 1446s, 1344s, 1241s, 1212s, 1138s, 1109s, 1028s, 753s, 601s; δ_H (500MHz, CDCl₃) 0.58-0.63 (1H, m), 0.70-0.78 (2H, m), 0.99-1.18 (5H, m), 1.29 (1H, br d, J 13Hz), 1.49 (1H, br d, J 12.5Hz), 1.57-1.62 (3H, m), 2.07-2.13 (1H, m, C(3)H), 2.23 (3H, s, NCH₃), 3.16 (1H, dd, J 12.5, 4.5Hz, C(2)H), 3.29 (1H, dd, J 12.5, 3.5Hz, C(2)H), 3.55 (1H, d, J 14.5Hz, C(5)H), 3.82 (3H, s, OCH₃), 3.84 (1H, d, J 14.5Hz, C(5)H), 3.93 (3H, s, OCH₃), 4.19 (1H, d, J 12Hz, C(10)H), 4.60 (1H, d, J 12Hz, C(10)H), 6.65 (1H, s, aryl CH), 6.88 (1H, s, aryl CH), 7.21 (1H, d, J 8Hz, aryl CH), 7.32-7.38 (3H, m, aryl CH); δ_c (100MHz, CDCl₃) 26.46, 26.51, 26.88, 33.27, 34.03, 34.75, 35.40, 39.32, 56.13, 56.17, 59.14, 60.33, 73.91, 74.08, 112.27, 113.93, 127.62, 128.09, 129.61, 130.35, 131.36, 133.43, 138.93, 143.02, 147.26, 147.51; m/z (ES) 410

(MH⁺, 100%); HRMS found 410.2714, C₂₆H₃₆NO₃ (MH⁺) requires 410.2695.

(M,10S)-10-Cyclohexylmethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(M)-4q.** Colorless crystals; thermodynamic dr: 1:11 (*P:M*); m.p. 167-169°C (EtOH); R_f 0.35 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 90:7:3); ν_{max} (KBr disc)/cm⁻¹ 2921s, 2847s, 1514s, 1242s, 1207s, 1142s, 1090s, 755s; δ_H (500MHz, CDCl₃) 0.69-0.76 (1H, m), 0.85-0.93 (2H, m), 1.06-1.29 (4H, m), 1.37-1.43 (1H, m), 1.56-1.69 (5H, m), 2.32 (3H, s, NCH₃), 3.15 (1H, dd, J 12.5, 8.5Hz, C(2)H), 3.19-3.22 (1H, m, C(3)H), 3.52 (1H, d, J 12.5Hz, C(5)H), 3.76 (1H, dd, J 12.5, 10Hz, C(2)H), 3.85 (3H, s, OCH₃), 3.96 (3H, s, OCH₃), 3.98 (1H, d, J 12.5Hz, C(5)H), 4.25-4.32 (2H, ABq, J 10Hz, C(10)H₂), 6.58 (1H, s, aryl CH), 7.15 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.44-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 26.71, 26.81, 27.01, 33.76, 34.45, 34.74, 35.60, 38.14, 48.02, 56.17, 56.24, 57.63, 68.11, 69.30, 112.08, 113.15, 127.90, 128.40, 130.22, 130.50, 131.04, 133.31, 135.47, 142.02, 147.44, 148.68; m/z (ES) 410 (MH⁺, 100%); HRMS found 410.2714, C₂₆H₃₆NO₃ (MH⁺) requires 410.2695.

(P,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(P)-4r.** Colorless oil; yield: 97%; kinetic dr: 35:1 (*P:M*); R_f 0.40 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 87:10:3); ν_{max} (thin film)/cm⁻¹ 2952s, 2866s, 1605m, 1515s, 1485s, 1464s, 1239s, 1212s, 1138s, 1111s, 1096s, 1046s, 913s, 732s; δ_H (500MHz, CDCl₃) 0.60 (3H, d, J 6.5Hz, CHCH₃), 0.69-0.74 (1H, m, CHH'CH(CH₃)₂), 0.77 (3H, d, J 6.5Hz, CHCH₃), 1.02-1.08 (1H, m, CHH'CH(CH₃)₂), 1.44-1.52 (1H, m, CH(CH₃)₂), 2.05-2.10 (1H, m, C(3)H), 2.26 (3H, s, NCH₃), 3.16 (1H, dd, J 12.5, 4.5Hz, C(2)H), 3.34 (1H, dd, J 12.5, 10Hz, C(2)H), 3.59 (1H, d, J 14.5Hz, C(5)H), 3.85 (3H, s, OCH₃), 3.88 (1H, d, J 14.5Hz, C(5)H), 3.95 (3H, s, OCH₃), 4.20 (1H, d, J 12Hz, C(10)H), 4.68 (1H, d, J 12Hz, C(10)H), 6.69 (1H, s, aryl CH), 6.89 (1H, s, aryl CH), 7.23 (1H, d, J 7Hz, aryl CH), 7.34-7.41 (3H, m, aryl CH); δ_c (100MHz, CDCl₃) 22.54 & 23.50 (CH(CH₃)₂), 25.29 (CH(CH₃)₂), 34.87 (NCH₃), 40.79 (CH₂CH(CH₃)₂), 56.16 & 56.22 (OCH₃), 59.46 (C5), 61.02 (C3), 74.01 (C2 & C10), 112.21, 113.99, 127.62, 128.06, 129.57 & 130.31 (6 x CH), 131.22, 133.46, 138.91, 143.00, 147.21 & 147.40 (6 x quaternary); m/z (ES) 370 (MH⁺, 100%); HRMS found 370.2368, C₂₃H₃₂NO₃ (MH⁺) requires 370.2382.

(M,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; **(M)-4r.** Colorless crystals; thermodynamic dr: 1:10 (*P:M*); m.p. 146-147°C (EtOH); R_f 0.32 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 93:5:2); ν_{max} (KBr disc)/cm⁻¹ 2951s, 2847s, 1513s, 1242s, 1207s, 1141s, 1090s, 755s; δ_H (500MHz, CDCl₃) 0.76 (3H, d, J 6.5Hz, CHCH₃), 0.78-0.81 (1H, m, CHH'CH(CH₃)₂), 0.88 (3H, d, J 7Hz, CHCH₃), 1.25-1.31 (1H, m, CHH'CH(CH₃)₂), 1.75-1.80 (1H, m, CH(CH₃)₂), 2.34 (3H, s, NCH₃), 3.15 (1H, dd, J 13.5, 3.5Hz, C(2)H), 3.16-3.21 (1H, m, C(3)H), 3.53 (1H, d, J 12.5Hz, C(5)H), 3.79 (1H, dd, J 12.5, 10.5Hz, C(2)H), 3.85 (3H, s, OCH₃), 3.93 (3H, s, OCH₃), 4.00 (1H, d, J 12.5Hz, C(5)H), 4.29 (2H, ABq, J 10Hz, C(10)H₂), 6.59 (1H, s, aryl CH), 7.16 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.31 & 24.08 (CH(CH₃)₂), 25.11 (CH(CH₃)₂), 35.46 (NCH₃), 39.24 (CH₂CH(CH₃)₂), 48.61 (C3), 55.98 & 56.12 (OCH₃), 57.65 (C5), 68.14 & 69.44 (C2 & C10), 112.04, 113.11, 127.89 & 128.44 (4 x CH), 130.30 (quaternary), 130.57 & 131.10 (2 x CH), 133.29, 135.49, 142.01, 147.44 & 148.63 (5 x

quaternary); m/z (ES) 370 (MH^+ , 100%). Found: C, 75.0; H, 8.55; N, 3.8%. $\text{C}_{23}\text{H}_{31}\text{NO}_3$ requires C, 74.8; H, 8.45; N, 3.8%.

(M,10R)-10-Ethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4s. Colorless oil; yield: 91%; kinetic dr: 1:25 ($P:M$); R_f 0.30 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 90:7:3); ν_{max} (thin film)/ cm^{-1} 2932s, 1605m, 1515s, 1464s, 1244s, 1210s, 1138s, 1028s, 756m; δ_{H} (500MHz, CDCl_3) 0.73 (3H, t, J 7.5Hz, CH_2CH_3), 1.12-1.25 (2H, m, CH_2CH_3), 1.96-2.01 (1H, m, C(3)H), 2.28 (3H, s, NCH_3), 3.24 (1H, dd, J 12.5, 9.5Hz, C(2)H), 3.31 (1H, dd, J 12.5, 4Hz, C(2)H), 3.49 (1H, d, J 14.5Hz, C(5)H), 3.81 (3H, s, OCH_3), 3.87 (1H, d, J 14.5Hz, C(5)H), 3.93 (3H, s, OCH_3), 4.25 (1H, d, J 12Hz, C(10)H), 4.42 (1H, d, J 12Hz, C(10)H), 6.61 (1H, s, aryl CH), 7.02 (1H, s, aryl CH), 7.19 (1H, dd, J 6.5, 2Hz, aryl CH), 7.29-7.37 (3H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 11.05 (CH_2CH_3), 24.36 (CH_2CH_3), 38.12 (NCH_3), 56.08 & 56.13 (OCH_3), 58.48 (C5), 65.30 (C3), 73.75 (C2 & C10), 112.30, 113.65, 127.60, 128.12, 129.41 & 130.35 (6 x CH), 132.17, 132.91, 138.68, 142.94, 147.11 & 147.74 (6 x quaternary); m/z (ES) 342 (MH^+ , 100%); HRMS found 342.2085, $\text{C}_{21}\text{H}_{26}\text{NO}_3$ (MH^+) requires 342.2069.

(P,10R)-10-Ethyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4s. Colorless crystals; thermodynamic dr: 9:1 ($P:M$); m.p. 136-138°C (EtOH); R_f 0.17 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 90:7:3); ν_{max} (KBr disc)/ cm^{-1} 2934s, 2845s, 1605m, 1513s, 1464s, 1241s, 1207s, 1141s, 1091s, 755s; δ_{H} (500MHz, CDCl_3) 0.95 (3H, t, J 7Hz, CH_2CH_3), 1.03-1.18 (1H, m, CHHCH_3), 1.23-1.30 (1H, m, CHHCH_3), 2.33 (3H, s, NCH_3), 3.03-3.08 (1H, m, C(3)H), 3.19 (1H, dd, J 12.5, 4Hz, C(2)H), 3.55 (1H, d, J 12.5Hz, C(5)H), 3.80 (1H, dd, J 12, 10.5Hz, C(2)H), 3.85 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 4.03 (1H, d, J 12.5Hz, C(5)H), 4.21-4.31 (2H, ABq, J 9.5Hz, C(10)H), 6.59 (1H, s, aryl CH), 7.19 (1H, s, aryl CH), 7.20 (1H, dd, J 9, 5Hz, aryl CH), 7.35-7.39 (2H, m, aryl CH), 7.42-7.45 (1H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 11.74, 22.00, 35.04, 51.85, 56.11, 56.17, 57.57, 68.27, 69.58, 112.07, 113.00, 127.87, 128.46, 130.41, 130.57, 131.04, 133.15, 135.43, 141.89, 147.36, 148.63; m/z (ES) 342 (MH^+ , 100%); HRMS found 342.2081, $\text{C}_{21}\text{H}_{26}\text{NO}_3$ (MH^+) requires 342.2069.

(M,10R)-4,5-Dimethoxy-9,10-dimethyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (M)-4t. Colorless oil; yield: 94%; kinetic dr: 1:32 ($P:M$); R_f 0.15 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 90:7:3); ν_{max} (thin film)/ cm^{-1} 2931s, 2847s, 1605m, 1514s, 1463s, 1247s, 1209s, 1138s, 1110s, 1028s, 758s, 733s; δ_{H} (500MHz, CDCl_3) 0.82 (3H, d, J 7Hz, C(3)CH₃), 2.27-2.31 (1H, m, C(3)H), 2.29 (3H, s, NCH_3), 3.17 (1H, dd, J 12, 9.5Hz, C(2)H), 3.28 (1H, dd, J 12, 3.5Hz, C(2)H), 3.43 (1H, d, J 14.5Hz, C(5)H), 3.82 (3H, s, OCH_3), 3.89 (1H, d, J 14.5Hz, C(5)H), 3.93 (3H, s, OCH_3), 4.28 (1H, d, J 11.5Hz, C(10)H), 4.42 (1H, d, J 11.5Hz, C(10)H), 6.60 (1H, s, aryl CH), 7.01 (1H, s, aryl CH), 7.18-7.20 (1H, m, aryl CH), 7.32-7.36 (3H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 17.49 (C(3)CH₃), 38.93 (NCH_3), 56.25 (OCH_3), 57.86 (C5), 59.38 (C3), 73.72 & 75.06 (C2 & C10), 112.39, 113.46, 127.59, 128.01, 129.31 & 130.19 (6 x CH), 131.76, 132.89, 138.48, 142.70, 147.05 & 147.67 (6 x quaternary); m/z (ES) 328 (MH^+ , 100%); HRMS found 328.1898, $\text{C}_{20}\text{H}_{26}\text{NO}_3$ (MH^+) requires 328.1912.

(P,10R)-4,5-Dimethoxy-9,10-dimethyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaene; (P)-4t. Colorless oil; thermodynamic dr: 6:1 ($P:M$); R_f 0.13 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 77:20:3); ν_{max} (thin film)/ cm^{-1} 2933s, 2845s, 1605m, 1513s, 1242s, 1208s, 1141s, 1092s, 1077s, 756s; δ_{H}

(500MHz, CDCl_3) 0.89 (3H, d, J 7Hz, C(3)CH₃), 2.39 (3H, s, NCH_3), 3.20 (1H, dd, J 12.5, 4Hz, C(2)H), 3.34-3.38 (1H, m, C(3)H), 3.53 (1H, d, J 12.5Hz, C(5)H), 3.78 (1H, dd, J 12.5, 10.5Hz, C(2)H), 3.85 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 3.97 (1H, d, J 12.5Hz, C(5)H), 4.24-4.32 (2H, ABq, J 9.5Hz, C(10)H), 6.59 (1H, s, aryl CH), 7.14 (1H, s, aryl CH), 7.19-7.21 (1H, m, aryl CH), 7.35-7.40 (2H, m, aryl CH), 7.43-7.45 (1H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 15.91 (C(3)CH₃), 35.49 (NCH_3), 46.67 (C3), 56.18 & 56.43 (OCH_3), 57.67 (C5), 68.36 & 69.85 (C2 & C10), 111.60, 113.11, 127.90 & 128.44 (4 x CH), 130.19 (quaternary), 130.53 & 131.01 (2 x CH), 133.26, 135.49, 141.87, 147.45 & 148.86 (5 x quaternary); m/z (ES) 328 (MH^+ , 100%); HRMS found 328.1898, $\text{C}_{20}\text{H}_{26}\text{NO}_3$ (MH^+) requires 328.1912.

(P,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (P)-4u. Colorless oil; yield: 93%; kinetic dr: 2:1 ($P:M$); R_f 0.23 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 93:5:2); ν_{max} (thin film)/ cm^{-1} 2952s, 1599m, 1518s, 1488s, 1464s, 1265s, 1214s, 1138s, 1046s, 750m; δ_{H} (500MHz, CDCl_3) 0.80 (3H, d, J 6.5Hz, CHCH_3), 0.86 (3H, d, J 6.5Hz, CHCH_3), 0.88-0.93 (1H, m, C(3)CHH), 1.25-1.31 (1H, m, C(3)CHH), 1.67-1.75 (1H, m, $\text{CH}(\text{CH}_3)_2$), 2.30 (3H, s, NCH_3), 2.94-3.00 (1H, m, C(3)H), 3.41 (1H, d, J 14.5Hz, C(5)H), 3.86 (3H, s, OCH_3), 3.89-3.94 (1H, m, C(2)H), 3.92 (3H, s, OCH_3), 3.94 (1H, d, J 14.5Hz, C(5)H), 4.11 (1H, dd, J 12, 3Hz, C(2)H), 6.74 (1H, s, aryl CH), 6.88 (1H, s, aryl CH), 7.09-7.36 (4H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 22.47 & 23.66 ($\text{CH}(\text{CH}_3)_2$), 25.48 ($\text{CH}(\text{CH}_3)_2$), 33.22 (NCH_3), 39.26 (C(3)CH₂), 56.15 & 56.38 (OCH_3), 60.71 (C5), 61.56 (C3), 70.83 (C2), 113.00, 115.14, 117.86, 122.90 & 128.90 (5 x CH), 130.06 (quaternary), 130.57 (CH), 131.82, 134.43, 147.29, 148.01 & 155.88 (5 x quaternary); m/z (ES) 356 (MH^+ , 100%); HRMS found 356.2209, $\text{C}_{22}\text{H}_{30}\text{NO}_3$ (MH^+) requires 356.2225.

(M,10S)-10-Isobutyl-4,5-dimethoxy-9-methyl-12-oxa-9-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,4,6,14,16-hexaene; (M)-4u. Colorless oil; R_f 0.23 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 93:5:2); δ_{H} (500MHz, CDCl_3) 0.86 (3H, d, J 6.5Hz, CHCH_3), 0.88 (3H, d, J 7Hz, CHCH_3), 0.90-1.03 (1H, m, C(3)CHH), 1.36-1.42 (1H, m, C(3)CHH), 1.67-1.75 (1H, m, $\text{CH}(\text{CH}_3)_2$), 2.04 (3H, s, NCH_3), 3.03-3.09 (1H, m, C(3)H), 3.05 (1H, d, J 12.5Hz, C(5)H), 3.62 (1H, d, J 12.5Hz, C(5)H), 3.87 (3H, s, OCH_3), 3.89-3.96 (2H, m, C(2)H), 3.91 (3H, s, OCH_3), 6.75 (1H, s, aryl CH), 7.00 (1H, d, J 8Hz, aryl CH), 7.09-7.36 (4H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 22.04 & 23.88 ($\text{CH}(\text{CH}_3)_2$), 25.29 ($\text{CH}(\text{CH}_3)_2$), 35.96 (NCH_3), 39.87 (C(3)CH₂), 56.10 & 56.33 (OCH_3), 58.14 (C3), 58.54 (C5), 74.13 (C2), 112.25, 112.45, 120.53, 123.28, 129.04 & 129.61 (6 x CH), 129.62, 132.34, 135.40, 147.96, 148.24 & 158.66 (6 x quaternary); m/z (ES) 356 (MH^+ , 100%); HRMS found 356.2209, $\text{C}_{22}\text{H}_{30}\text{NO}_3$ (MH^+) requires 356.2225.

rel-(P,4S,9S)-3-Oxa-10-azatetracyclo[16.4.0.0^{4,9}.0^{12,17}]docosa-12,14,16,18,20,22-hexaene; 4v. Colorless oil; yield: 77%; kinetic dr: 11:1 [rel -(P,4S,9S): rel -(M,4S,9S)]; R_f 0.50 (SiO_2 ; Hexane: EtOAc: 1:1); ν_{max} (thin film)/ cm^{-1} 2929s, 2856s, 1448s, 1089s, 755s; δ_{H} (500MHz, CDCl_3) 0.93 (1H, m), 1.03-1.12 (2H, m), 1.23 (1H, m), 1.57 (1H, m), 1.63 (1H, m), 1.86 (1H, m), 1.98 (1H, m), 2.04 (1H, m, C(3)H), 2.17 (3H, s, NCH_3), 2.54 (1H, m, C(2)H), 3.48 (1H, d, J 14.5Hz, C(5)H), 3.90 (1H, d, J 14.5Hz, C(5)H), 3.97 (1H, d, J 11.5Hz, C(10)H), 4.58 (1H, d, J 11.5Hz, C(10)H), 7.09 (1H, dd, J 7.5, 1Hz, aryl CH), 7.17 (1H, m, aryl CH), 7.26-7.39 (5H, m, aryl CH), 7.59 (1H, d, J 7.5Hz, aryl CH); δ_{C} (125MHz, CDCl_3) 24.65, 25.19, 29.16, 33.83, 45.32 (NCH_3), 55.53 (C5), 67.64 (C3), 72.03 (C10), 82.93 (C2), 126.04,

127.18, 127.21, 127.40, 128.48, 129.21, 129.48, 129.84, 138.18, 140.59, 140.99, 142.52; m/z (ES) 308 (MH^+ , 100%); HRMS found 308.2027, $C_{21}H_{26}NO$ (MH^+) requires 308.2014.

rel-(3S,8S)-2-Oxa-9-azatetracyclo[15.4.0.0^{3,8}.0^{11,16}]uncosa-11,13,15,17,19,21-hexaene; 4w. Colorless oil; yield: 96%; kinetic dr: >50:1 [*rel*-(*P*,3S,8S): *rel*-(*M*,3S,8S)]; R_f 0.37 (SiO₂; Hexane: EtOAc: Et₃N; 82:17:1); ν_{max} (thin film)/cm⁻¹ 2926s, 2786s, 1473s, 1242s, 1028s, 984s, 745s; δ_H (500MHz, CDCl₃) 0.46-0.68 (3H, m), 0.93 (1H, m), 1.00-1.11 (2H, m), 1.18 (1H, m), 1.45 (3H, s, NCH₃), 1.77 (1H, m), 2.36 (1H, m, C(3)H), 3.16 (1H, d, J14Hz, C(5)H), 3.28 (1H, m, C(2)H), 3.33 (1H, d, J14Hz, C(5)H), 6.57 (1H, d, J8Hz, aryl CH), 6.63 (1H, m, aryl CH), 6.77-6.97 (6H, m, aryl CH); δ_C (125MHz, CDCl₃) 24.60, 24.97, 25.81, 32.65, 35.33 (NCH₃), 59.29 (C5), 63.06 (C3), 82.39 (C2), 118.15, 121.49, 126.89, 127.09, 127.78, 128.98, 129.53, 130.55, 136.09, 138.25, 140.95, 159.79; m/z (ES) 294 (MH^+ , 100%); HRMS found 294.1849, $C_{20}H_{24}NO$ (MH^+) requires 294.1858.

(M,3S)-17-Bromo-5-methyl-3-phenyl-2-oxa-5-azatricyclo[11.4.0.0^{7,12}]heptadeca-7,9,11,13,15,17-hexaene; (M)-4x. Colorless oil; yield: 81%; kinetic dr: 1:>50 (*P:M*); R_f 0.48 (SiO₂; Hexane: EtOAc: Et₃N; 90:9:1); ν_{max} (thin film)/cm⁻¹ 2926s, 2838s, 2788s, 1495s, 1430s, 1073s, 1012s, 755s, 699s; δ_H (500MHz, CDCl₃) 2.34 (3H, s, NCH₃), 2.53 (1H, d, J15Hz, C(3)H), 3.09 (1H, dd, J15, 9Hz, C(3)H), 3.44 (1H, d, J13Hz, C(5)H), 3.53 (1H, d, J13Hz, C(5)H), 5.24 (1H, d, J9Hz, C(2)H), 6.96 (1H, t, J7.5Hz, aryl CH), 7.06 (1H, dd, J7.5, 2Hz, aryl CH), 7.18-7.36 (9H, m, aryl CH), 7.51 (1H, dd, J8, 2Hz, aryl CH); δ_C (125MHz, CDCl₃) 43.27 (NCH₃), 59.24 (C5), 61.84 (C3), 81.26 (C2), 115.20, 124.15, 125.86, 127.20, 127.35, 127.72, 128.13, 128.17, 129.66, 130.05, 132.75, 136.57, 138.91, 139.88, 141.20, 154.77; m/z (ES) 394 (MH^+ , 100%); HRMS found 394.0815, $C_{22}H_{21}BrNO$ (MH^+) requires 394.0806.

(P,6S)-6-Phenyl-5-oxa-8-azatetracyclo[15.4.0.0^{4,16}.0^{10,15}]uncosa-1,3,10,12,14,16,18,20-octaene; (P)-4y. White solid; yield: 73%; kinetic dr: 1.5:1 (*P:M*); m.p. 60°C; R_f 0.50 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 82:17:1); ν_{max} (KBr disc)/cm⁻¹ 2923s, 1458s, 1385s, 1209s, 1018s, 748s, 698s; δ_H (500MHz, CDCl₃) 2.36 (3H, s, NCH₃), 3.10 (1H, dd, J15, 3.5Hz, C(3)H), 3.25 (1H, dd, J15, 6.5Hz, C(3)H), 3.52 (1H, d, J13.5Hz, C(5)H), 3.62 (1H, d, J13.5Hz, C(5)H), 5.09 (1H, dd, J6.5, 3.5Hz, C(2)H), 7.10 (1H, d, J9Hz, aryl CH), 7.20 (1H, d, J8Hz, aryl CH), 7.28-7.49 (11H, m, aryl CH), 7.52 (1H, d, J9Hz, aryl CH), 7.83 (1H, d, J8Hz, aryl CH); δ_C (100MHz, CDCl₃) 43.23 (NCH₃), 60.49, 63.19, 77.69 (C2), 122.91, 124.36, 125.23, 126.37, 126.51, 126.68, 127.83, 127.92, 128.05, 128.18, 128.68, 128.97, 130.19, 131.18, 131.56, 134.21, 136.40, 137.92, 142.40, 152.14; m/z (ES) 366 (MH^+ , 100%); HRMS found 366.1872, $C_{26}H_{24}NO$ (MH^+) requires 366.1858.

(M,6S)-6-Phenyl-5-oxa-8-azatetracyclo[15.4.0.0^{4,16}.0^{10,15}]uncosa-1,3,10,12,14,16,18,20-octaene; (M)-4y. White solid; R_f 0.38 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 82:17:1); m.p. 141°C; ν_{max} (KBr disc)/cm⁻¹ 2939s, 2787s, 1448s, 1329s, 1232s, 1020s, 761s, 748s; δ_H (500MHz, CDCl₃) 2.48 (3H, s, NCH₃), 2.81 (1H, d, J15Hz, C(3)H), 3.20 (1H, d, J12.5Hz, C(5)H), 3.31 (1H, dd, J15, 7Hz, C(3)H), 3.64 (1H, d, J12.5Hz, C(5)H), 5.10 (1H, d, J7Hz, C(2)H), 7.13 (1H, d, J9Hz, aryl CH), 7.26-7.46 (10H, m, aryl CH), 7.62-7.65 (2H, m, aryl CH), 7.81-7.87 (2H, m, aryl CH); δ_C (125MHz, CDCl₃) 44.52 (NCH₃), 57.45 (C3), 63.17 (C5), 82.03 (C2), 120.14, 124.41, 125.54, 125.77, 126.31, 127.11, 127.31, 127.51, 128.13, 128.47, 128.52, 129.62, 130.38, 130.75, 131.12, 132.86, 136.93, 137.33, 142.23, 154.22; m/z (ES) 366

(MH^+ , 100%); HRMS found 366.1872, $C_{26}H_{24}NO$ (MH^+) requires 366.1858.

(M,3S,4R)-4,5-Dimethyl-3-phenyl-2-oxa-5-azatricyclo[11.4.0.0^{7,12}]heptadeca-7,9,11,13,15,17-hexaene; (M)-4z. Colorless oil; yield: 68%; kinetic dr: 1:10 (*P:M*); R_f 0.42 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 82:17:1); ν_{max} (thin film)/cm⁻¹ 2935s, 2762s, 1480s, 1228s, 1011s, 740s, 700s; δ_H (500MHz, CDCl₃) 0.72 (3H, d, J7Hz, C(3)HCH₃), 2.67 (3H, s, NCH₃), 3.01 (1H, q, J7Hz, C(3)H), 3.38 (1H, d, J13.5Hz, C(5)H), 3.67 (1H, d, J13.5Hz, C(5)H), 5.22 (1H, s, C(2)H), 6.80 (1H, m, aryl CH), 7.13-7.39 (11H, m, aryl CH), 7.68 (1H, m, aryl CH); δ_C (125MHz, CDCl₃) 14.14 (C(3)CH₃), 47.27 (NCH₃), 57.05 (C5), 69.27 (C3), 82.55 (C2), 118.77, 123.70, 125.61, 126.95, 127.09, 127.29, 128.32, 129.13, 129.40, 129.88, 130.54, 134.02, 138.22, 138.26, 142.47, 156.85; m/z (ES) 330 (MH^+ , 100%); HRMS found 330.1872, $C_{23}H_{24}NO$ (MH^+) requires 330.1858.

(2) Method B. An oven-dried, three-necked round-bottomed flask containing the cyclization precursor and equipped with a magnetic stirring bar, a septum, a low temperature thermometer and a vacuum/gas inlet (greased joints) was evacuated and twice heated with a heat gun over 30 minutes. The flask was filled with argon and charged with anhydrous 2-methyltetrahydrofuran (2-MeTHF, 0.01-0.05M). The solution was cooled to 0°C and a preformed solution of *i*-PrBu₂MgLi (2.2 equiv.)²⁷ was added *via* a cannula. After addition the reaction was stirred for 4 hours at 0°C to give a clear yellow solution. A freshly prepared solution of CuCN·2LiBr (1M) in 2-MeTHF (1.1 equiv.)²⁸ was added dropwise, the mixture was stirred for 1 hour and then a freshly prepared solution of 1,3-dinitrobenzene (1M) in 2-MeTHF (4.0 equiv.) was added to give a dark brown-black solution. The solution was allowed to warm to room temperature over 1-12 hours. The black solution was concentrated *in vacuo* and partitioned between an aqueous solution of NaOH (1M) and EtOAc. The resulting two-phase mixture was separated and the aqueous phase was extracted three times with EtOAc. The combined organic layers were washed (saturated aqueous NaCl), dried (K₂CO₃), filtered, concentrated *in vacuo* and chromatographed.

Synthesis of (S)-12-Benzyl-17,18-dimethoxy-13-methyl-10-oxa-13-aza-2-mercurotricyclo[13.4.0.0^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 8. The dilithium intermediate was prepared from **3e** as described in the general procedure above. To the clear yellow solution a freshly prepared solution of dry HgBr₂ (1.0 equiv.) in anhydrous 2-MeTHF (*ca.* 2ml) was added dropwise, then the mixture was stirred for 12 hours allowing the reaction temperature to rise slowly to room temperature. Water and Et₂O was added and the resulting two-phase mixture was separated, and then the aqueous phase was extracted three times with Et₂O. The combined organic layers were dried (MgSO₄), filtered, concentrated *in vacuo* and recrystallized from EtOH to give **8** (65%) as colorless crystals; m.p. 156.5-157.5°C (EtOH); R_f 0.32 (base-washed SiO₂; Hexane: EtOAc: Et₃N; 80:15:5); ν_{max} (KBr disc)/cm⁻¹ 2831s, 1498s, 1458s, 1248s, 1208s, 1158s, 1104s, 1048s, 1030s, 737s, 697s; δ_H (500MHz, CDCl₃) 2.26 (3H, s, NCH₃), 2.35 (1H, dd, J13, 10.5Hz, PhCHH'), 3.10 (1H, br d, J12Hz, PhCHH'), 3.36-3.42 (1H, m, C(3)H), 3.52 (1H, dd, J11, 3.5Hz, C(2)H), 3.65-3.73 (2H, br m, C(2)H & C(5)H), 3.90 (3H, s, OCH₃), 3.94 (3H, s, OCH₃), 3.94-4.00 (1H, br m, C(5)H), 4.29 (1H, d, J11Hz, C(10)H), 4.62 (1H, d, J11Hz, C(10)H), 6.85 (1H, s, aryl CH), 7.13 (1H, s, aryl CH), 7.15-7.33 (8H, m, aryl CH), 7.55 (1H, d, J7.5Hz, aryl CH); δ_C (100MHz, CDCl₃) 31.20, 56.11, 56.35, 64.75, 69.08, 74.51,

(27) To a solution of *i*-PrMgCl (1.0 equiv.) in 2-MeTHF at 0°C was added *n*-BuLi (2.0 equiv.) and the mixture stirred for 30 minutes to give a clear, pale yellow solution.

(28) Two equivalents of CuCN can be used without effecting the reaction yield or selectivity.

112.48, 121.53, 126.38, 127.18, 127.26, 127.61, 128.78, 129.14, 138.92, 139.79, 140.04, 145.72, 147.23, 148.08, 160.32; m/z (ES) 602 (MH^+ , ^{198}Hg , 14%), 603 (MH^+ , ^{199}Hg , 40%), 604 (MH^+ , ^{200}Hg , 72%), 605 (MH^+ , ^{201}Hg , 38%), 606 (MH^+ , ^{202}Hg , 100%), 607 (MH^+ , ^{202}Hg , ^{13}C , 10%), 608 (MH^+ , ^{204}Hg , 10%); HRMS found 606.1929, $C_{26}H_{30}HgNO_3$ (MH^+) requires 606.1932.

Synthesis of 9 & 10. The dilithium intermediate was prepared from **3e** as described in the general procedure above. To the clear yellow solution a freshly prepared solution of Me_2SiCl_2 or Ph_2SiCl_2 (1.0 equiv.) in anhydrous 2-MeTHF (ca. 5ml) was added dropwise, then the mixture was stirred for 12 hours allowing the reaction temperature to slowly rise to room temperature. A solution of 10% NH_4OH in saturated aqueous NH_4Cl was added and the resulting two-phase mixture separated and the aqueous phase was extracted twice with CH_2Cl_2 . The combined organic layers were dried (K_2CO_3), filtered, concentrated *in vacuo* and chromatographed to give **9** (86%) or **10** (80%) as colorless oils.

(S)-12-Benzyl-17,18-dimethoxy-2,2,13-trimethyl-10-oxa-13-aza-2-sila-tricyclo[13.4.0.0.3^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 9. R_f 0.41 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 80:15:5); ν_{max} (thin film)/ cm^{-1} 2949s, 2854s, 1593s, 1505s, 1455s, 1248s, 1207s, 1063s, 838s, 734s, 699s; δ_H (500MHz, $CDCl_3$) 0.28 (3H, s, $SiCH_3$), 0.34 (3H, s, $SiCH_3$), 1.87 (3H, s, NCH_3), 1.99 (1H, dd, $J_{9,5}$, 4Hz, $PhCHH'$), 2.46-2.52 (2H, m, $PhCHH'$ & C(3)H), 2.86 (1H, dd, $J_{11,5}$, 3Hz, C(2)H), 3.24 (1H, d, $J_{12,5Hz}$, C(5)H), 3.28-3.33 (1H, m, C(2)H), 3.48 (3H, s, OCH_3), 3.48 (1H, d, $J_{12,5Hz}$, C(5)H), 3.55 (3H, s, OCH_3), 3.95 (1H, d, $J_{10,5Hz}$, C(10)H), 4.05 (1H, d, $J_{10,5Hz}$, C(10)H), 6.53 (1H, s, aryl CH), 6.74 (2H, d, $J_{7,5Hz}$, aryl CH), 6.78 (1H, s, aryl CH), 6.83-6.98 (5H, m, aryl CH), 7.03 (1H, d, $J_{4,5Hz}$, aryl CH), 7.29-7.31 (1H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 0.00 & 0.35 ($SiCH_3$), 31.40 ($PhCH_2$), 33.41 (NCH_3), 53.23 & 53.45 (OCH_3), 57.62 (C5), 60.95 (C3), 65.26 & 70.91 (C2 & C10), 110.44, 115.24, 123.32, 124.64, 125.69, 126.42 & 126.64 (7 x CH), 126.83 (quaternary), 127.26 (CH), 130.27 (quaternary), 132.76 (CH), 135.99, 137.36, 140.51, 144.36 & 146.60 (5 x quaternary); m/z (ES) 462 (MH^+ , 100%); HRMS found 462.2455, $C_{28}H_{36}NO_3Si$ (MH^+) requires 462.2464.

(S)-11-Benzyl-5,6-dimethoxy-10-methyl-2,2-diphenyl-13-oxa-10-aza-2-sila-tricyclo[13.4.0.0.0^{3,8}]nonadeca-1(15),3,5,7,16,18-hexaene; 10. R_f 0.27 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 85:10:5); ν_{max} (thin film)/ cm^{-1} 2933s, 2845s, 1591s, 1505s, 1463s, 1428s, 1373s, 1244s, 1065s, 740s, 700s; δ_H (500MHz, $CDCl_3$) 2.30 (3H, s, NCH_3), 2.50 (1H, dd, $J_{13,5}$, 7.5Hz, $PhCHH'$), 2.81 (1H, dd, $J_{13,5}$, 6.5Hz, $PhCHH'$), 3.27-3.31 (2H, m, C(2)H & C(3)H), 3.33 (1H, d, J_{14Hz} , C(5)H), 3.59 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.76-3.82 (1H, m, C(2)H), 3.96 (1H, d, $J_{10,5Hz}$, C(10)H), 4.03 (1H, d, J_{14Hz} , C(5)H), 4.73 (1H, d, $J_{10,5Hz}$, C(10)H), 6.85 (1H, s, aryl CH), 7.16 (1H, s, aryl CH), 7.17-7.65 (19H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 37.18, 37.81, 55.70, 56.02, 61.89, 63.77, 70.02, 72.00, 112.61, 120.40, 126.22, 127.11, 127.74, 127.85, 127.91, 128.39, 128.52, 128.55, 129.21, 129.47, 130.09, 131.35, 134.49, 135.49, 136.23, 136.51, 136.63, 137.97, 139.20, 140.04, 140.96, 145.29, 146.62, 150.24; m/z (ES) 586 (MH^+ , 100%); HRMS found 586.2781, $C_{38}H_{40}NO_3Si$ (MH^+) requires 586.2777.

Synthesis of Building Blocks.

(1) Synthesis of Benzyl Bromides.

Radical Bromination. A suspension of the toluene (1.0 equiv.), *N*-bromosuccinimide (1.0 equiv.) and benzoyl peroxide (0.004 equiv.) in CCl_4 (0.5-1M) was heated at reflux for 4 hours and then filtered while the solution was still hot. The filtrate was then

concentrated *in vacuo* and either recrystallized, distilled under reduced pressure, or chromatographed.

2-Bromo-1-bromomethyl-4-fluorobenzene; 19b. Colorless solid; yield: 72%; m.p. 49-51°C (lit.²⁹ 51-52°C); R_f 0.54 (SiO_2 ; Hexane); δ_H (500MHz, $CDCl_3$) 4.59 (2H, s, CH_2Br), 7.03 (1H, ddd, $J_{8,7.5}$, 2.5Hz, CH), 7.34 (1H, dd, $J_{8,2.5Hz}$, CH), 7.45 (1H, dd, $J_{8,5}$, 6Hz, CH); δ_C (100MHz, $CDCl_3$) 32.67 (CH_2), 115.45 (d, J_{21Hz}), 120.87 (d, J_{24Hz}), 124.98 (d, J_{10Hz}), 132.50 (d, J_{9Hz}), 133.43 (d, $J_{3.5Hz}$), 162.38 (d, J_{250Hz}). Found: C, 31.6; H, 1.90; Br, 59.5; F, 7.2%. $C_7H_5Br_2F$ requires C, 31.4; H, 1.90; Br, 59.7; F, 7.1%.

1-Bromo-2-bromomethylnaphthalene; 19c. Off-white crystals; yield: 75%; m.p. 104-106°C (lit.³⁰ 107-109°C); R_f 0.43 (SiO_2 ; Hexane); δ_H (500MHz, $CDCl_3$) 4.87 (2H, s, CH_2Br), 7.52-7.57 (2H, m, CH), 7.62 (1H, t, $J_{7,5Hz}$, CH), 7.79-7.83 (2H, m, CH), 8.34 (1H, d, J_{8Hz} , CH); δ_C (100MHz, $CDCl_3$) 34.76, 124.90, 127.12, 127.52, 127.62, 127.76, 128.06, 128.21, 132.38, 134.01, 134.81; m/z (EI) 298 (M^+ , ^{79}Br ^{79}Br , 30%), 300 (M^+ , ^{79}Br ^{81}Br , 60%), 302 (M^+ , ^{81}Br ^{81}Br , 30%). Found: C, 44.1; H, 2.60; Br, 53.2%. $C_{11}H_8Br_2$ requires C, 44.0; H, 2.70; Br, 53.3%.

3-Bromo-4-bromomethylthiophene; 19e.³¹ Colorless oil; yield: 75%; R_f 0.33 (SiO_2 ; Hexane); δ_H (500MHz, $CDCl_3$) 4.49 (2H, s, CH_2Br), 7.30 (1H, d, $J_{3,5Hz}$, C(5)H), 7.41 (1H, d, $J_{3,5Hz}$, C(2)H). Found: C, 23.6; H, 1.70; Br, 62.3; S, 12.6%. $C_5H_4Br_2S$ requires C, 23.5; H, 1.50; Br, 62.4; S, 12.5%.

2-Bromo-3-bromomethyl-5-chlorobenzo[b]thiophene; 19f. White solid; yield: 92%; m.p. 112.5-113.5°C; R_f 0.55 (SiO_2 ; Hexane); ν_{max} (KBr disc)/ cm^{-1} 1419s, 1209s, 1102s, 1040s, 968m, 866s, 804s, 664s; δ_H (500MHz, $CDCl_3$) 4.62 (2H, s, CH_2Br), 7.31 (1H, d, $J_{8,5Hz}$, C(6)H), 7.60 (1H, d, $J_{8,5Hz}$, C(7)H), 7.74 (1H, s, C(4)H); δ_C (100MHz, $CDCl_3$) 23.79, 119.46, 121.68, 123.20, 125.95, 131.01, 131.81, 137.92, 138.03; m/z (EI) 338 (M^+ , ^{79}Br ^{79}Br ^{35}Cl , 5%), 339 (M^+ , 6%), 340 (M^+ , 13%), 341 (M^+ , 16%), 342 (M^+ , 11%), 343 (M^+ , 12%), 260 ($[M-Br]^+$, 75%), 262 ($[M-Br]^+$, 100%), 264 ($[M-Br]^+$, 25%). Found: C, 31.8; H, 1.35; Br, 46.9; Cl, 10.3; S, 9.6%. $C_9H_5Br_2ClS$ requires C, 31.8; H, 1.50; Br, 46.9; Cl, 10.4; S, 9.4%.

1-Bromo-2-bromomethyl-4-chlorobenzene. White crystals; yield: 76%; m.p. 65-66.5°C (lit.³² 67-68°C); R_f 0.46 (SiO_2 ; Hexane); ν_{max} (KBr disc)/ cm^{-1} 1459s, 1432s, 1218s, 1199s, 1095s, 1032s, 895s, 883s, 719s, 622s, 569s, 513s, 497s; δ_H (500MHz, $CDCl_3$) 4.52 (2H, s, CH_2Br), 7.14 (1H, dd, $J_{8,5}$, 2.5Hz, C(5)H), 7.44 (1H, d, $J_{2,5Hz}$, C(3)H), 7.49 (1H, d, $J_{8,5Hz}$, C(6)H); δ_C (100MHz, $CDCl_3$) 32.24, 122.22, 130.11, 131.08, 133.72, 134.35, 138.63; m/z (EI) 282 (M^+ , ^{79}Br ^{79}Br ^{35}Cl , 15%), 284 (M^+ , 24%), 286 (M^+ , 13%), 203 ($[M-Br]^+$, 80%), 205 ($[M-Br]^+$, 100%).

Preparation of 5-bromo-6-bromomethylbenzo[1,3]dioxole; 19d. A round-bottomed flask, equipped with a magnetic stirring bar, containing piperonyl alcohol (5.0 g, 32.9 mmol) and AcOH (10 ml) at 0°C was charged slowly with a mixture of Br_2 (2.0 ml, 38.8 mmol) and AcOH (6 ml). The reaction mixture was stirred at room temperature for 10 hours during which time a white solid was precipitated. The mixture was filtered and the solid was washed with distilled water and dried *in vacuo* to give a white solid (8.47 g, 88%); m.p. 91.5-92.5°C (lit.³³ 88-89°C); R_f 0.33 (SiO_2 ; Hexane: EtOAc; 3:1); ν_{max} (KBr disc)/ cm^{-1} 1502s, 1485s, 1251s, 1212s, 1124s, 1037s, 931s, 867s, 559s; δ_H (500MHz, $CDCl_3$) 4.55 (2H, s, CH_2Br), 5.99 (2H, s, OCH_2O),

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6.91 (1H, s, CH), 7.00 (1H, s, CH); δ_{C} (100MHz, CDCl_3) 34.48, 102.33, 110.72, 113.32, 115.83, 130.12, 147.76, 148.92; m/z (EI) 292 (M^+ , ^{79}Br , 10%), 294 (M^+ , ^{79}Br ^{81}Br , 15%), 296 (M^+ , ^{81}Br ^{81}Br , 9%), 213 ($[\text{M}-\text{Br}]^+$, 98%), 215 ($[\text{M}-\text{Br}]^+$, 100%). Found: C, 32.9; H, 1.90; Br, 54.3%. $\text{C}_8\text{H}_6\text{Br}_2\text{O}_2$ requires C, 32.7; H, 2.05; Br, 54.4%.

(2) Synthesis of Benzaldehydes.

Preparation of 2-bromo-5-chlorobenzaldehyde;

18b. A round-bottomed flask, equipped with a magnetic stirring bar, containing *N*-methylmorpholine-*N*-oxide (1.87 g, 16.0 mmol, 2.0 equiv.), activated powdered 4Å molecular sieves (15 cm^3) and MeCN (50 ml) at 0°C was charged with 1-bromo-2-bromomethyl-4-chlorobenzene (2.27 g, 7.98 mmol). The reaction mixture was stirred at 0°C for 2 hours. The mixture was filtered through a pad of SiO_2 and the filtrate concentrated *in vacuo* to give a white solid (1.14 g, 65%); m.p. 68–70°C; R_f 0.21 (SiO_2 ; Hexane); ν_{max} (KBr disc)/ cm^{-1} 1692s, 1575m, 1455s, 1392m, 1248s, 1190s, 1092s, 1031s, 896s, 818s, 721s, 639m, 526m; δ_{H} (500MHz, CDCl_3) 7.42 (1H, dd, $J_{8,5}$, 2.5Hz, C(4) H), 7.59 (1H, d, $J_{8,5}$ Hz, C(3) H), 7.87 (1H, d, $J_{2,5}$ Hz, C(6) H), 10.29 (1H, s, CHO); δ_{C} (100MHz, CDCl_3) 124.80, 129.81, 134.58, 134.76, 135.19, 135.28, 190.54; m/z (EI) 217 (M^+ , ^{79}Br ^{35}Cl , 37%), 219 (M^+ , 48%), 138 ($[\text{M}-\text{Br}]^+$, 39%), 107 (100%), 109 (78%). Found: C, 38.4; H, 1.75; Br, 36.3; Cl, 16.0%. $\text{C}_7\text{H}_4\text{BrClO}$ requires C, 38.3; H, 1.85; Br, 36.4; Cl, 16.2%.

Preparation of 2-bromo-5-methoxybenzaldehyde; 18c. A round-bottomed flask, equipped with a magnetic stirring bar, containing 2-bromo-5-methoxybenzoic acid (10.0 g, 43.3 mmol), THF (20 ml) and Et_2O (50 ml) at room temperature was slowly charged with borane-dimethyl sulfide (4.11 ml, 1.0 equiv.). The reaction mixture was vigorously stirred and heated at reflux for 1 hour. The mixture was concentrated *in vacuo*, resuspended in CH_2Cl_2 (20 ml) and added dropwise to a vigorously stirred solution of pyridinium chlorochromate (10.3 g, 1.1 equiv.) in CH_2Cl_2 (65 ml). The suspension was stirred and heated at reflux for 1 hour. The mixture was allowed to cool to room temperature, diluted with Et_2O (150 ml) and filtered through a pad of SiO_2 . The solid residue was washed with Et_2O (3 x 50 ml) and passed through the same pad of SiO_2 . The combined organic layers were dried (MgSO_4), filtered, concentrated *in vacuo* and chromatographed using CH_2Cl_2 as an eluent to give a white solid (7.90 g, 85%); m.p. 75.5–76.5°C (lit.³⁴ 75–76°C); R_f 0.66 (SiO_2 ; Hexane: EtOAc; 4:1); ν_{max} (KBr disc)/ cm^{-1} 1675s, 1599m, 1570m, 1474s, 1303m, 1284s, 1198m, 1060m, 1015m, 933s, 865m, 820s, 754m, 648m, 598m; δ_{H} (500MHz, CDCl_3) 3.84 (3H, s, CH_3), 7.04 (1H, dd, J_9 , 3.5Hz, C(4) H), 7.41 (1H, d, $J_{3\text{H}}$, C(6) H), 7.53 (1H, d, $J_{9\text{H}}$, C(3) H), 10.31 (1H, s, CHO); δ_{C} (100MHz, CDCl_3) 56.02, 112.85, 118.17, 123.31, 134.11, 134.72, 159.37, 191.87; m/z (EI) 214 (M^+ , ^{79}Br , 100%), 216 (M^+ , ^{81}Br , 100%). Found: C, 44.7; H, 3.35; Br, 37.1%. $\text{C}_8\text{H}_7\text{BrO}_2$ requires C, 44.7; H, 3.30; Br, 37.2%.

(3) Synthesis of Amino Alcohols.

Preparation of (S)-1-(2-bromophenoxymethyl)-2-phenylethylamine; (S)-17i. A round-bottomed flask, equipped with a magnetic stirring bar, containing (S)-2-amino-3-phenyl-propan-1-ol (1.0 g, 6.61 mmol) and phthalic anhydride (0.98 g, 1.0 equiv.) was charged with xylene (20 ml). The reaction mixture was stirred and heated at reflux for 3 hours.³⁵ The mixture was concentrated *in vacuo*, resuspended in hexane: toluene (3:1; 50 ml) and recrystallized to give a white solid, which was added to a stirred mixture of 2-bromophenol (1.5 equiv.), triphenylphosphine (1.5 equiv.), 1,1'-(azodicarbonyl)dipiperidine (1.5 equiv.) and benzene (40 ml). The mixture was stirred at room

temperature for 3 days, washed with an aqueous NaOH solution (1M), dried (MgSO_4), filtered, concentrated *in vacuo* and chromatographed to give a white solid. The solid was dissolved in EtOH (10 ml) and hydrazine (1 ml) and the resulting solution was stirred at room temperature for 2 hours. The solution was concentrated *in vacuo*, partitioned between an aqueous solution of Na_2CO_3 (1M) and EtOAc, the resulting two-phase mixture was separated and then the aqueous phase was extracted three times with EtOAc. The combined organic layers were dried (K_2CO_3), filtered, concentrated *in vacuo* and chromatographed to give a colorless oil [1.1 g, 54% (3 steps)]; R_f 0.15 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 30:65:5); ν_{max} (thin film)/ cm^{-1} 3376m br, 3025m, 2925m, 1586m, 1481s, 1278s, 1248s, 1052s, 1030s, 745s, 701s; δ_{H} (500MHz, CDCl_3) 1.53 (2H, br s, NH_2), 2.76 (1H, dd, J_{13} , 8.5Hz, PhCHH), 2.96 (1H, dd, J_{13} , 6Hz, PhCHH), 3.46–3.51 (1H, m, NCH), 3.84 (1H, dd, J_9 , 6.5Hz, CHH'OArl), 3.98 (1H, dd, J_9 , 4Hz, CHH'OArl), 6.82–6.85 (2H, m, aryl CH), 7.21–7.25 (4H, m, aryl CH), 7.29–7.32 (2H, m, aryl CH), 7.53 (1H, dd, $J_{8,5}$, 1.5Hz, aryl CH); δ_{C} (100MHz, CDCl_3) 40.90 (CH_2), 52.44 (CH), 73.42 (CH_2), 112.59 (quaternary), 113.57, 122.27, 126.73, 128.72, 128.84, 129.55 & 133.52 (7 x CH), 138.71 & 155.32 (2 x quaternary); m/z (ES) 306 (MH^+ , ^{79}Br , 100%), 308 (MH^+ , ^{81}Br , 97%); HRMS found 306.0511, $\text{C}_{15}\text{H}_{17}\text{BrNO}$ (MH^+ , ^{79}Br) requires 306.0493. Found: C, 59.0; H, 5.35; Br, 25.9; N, 4.5%. $\text{C}_{15}\text{H}_{16}\text{BrNO}$ requires C, 58.8; H, 5.25; Br, 26.1; N, 4.6%.

Preparation of (S)-3-amino-4-naphthalen-2-ylbutan-1-ol; (S)-17j. A round-bottomed flask, equipped with a magnetic stirring bar, containing (S)-3-amino-4-naphthalen-2-yl-butyric acid (1.0 g, 3.76 mmol) and THF (5 ml) at room temperature was slowly charged with a solution of LiAlH_4 (357 mg, 2.5 equiv.) in THF (5 ml) [Caution! Flammable solid and hydrogen gas evolved]. The reaction mixture was stirred and heated at reflux for 16 hours. The mixture was cooled in an ice bath and diluted with Et_2O (15 ml). The reaction was quenched over 10 minutes with distilled water (2 ml), aqueous NaOH (2M, 2 ml) and distilled water (2 ml). The solution was stirred for 30 minutes and filtered. The filter cake was washed with EtOAc (3 x 15 ml) and the organic filtrates were combined, dried (K_2CO_3), concentrated *in vacuo* and chromatographed to give a white solid (760 mg, 94%); m.p. 56–58°C; R_f 0.22 (base-washed SiO_2 ; EtOAc: MeOH: Et_3N ; 85:10:5); $[\alpha]_{\text{D}} -16.0$ (c=2.5, CH_2Cl_2); ν_{max} (KBr disc)/ cm^{-1} 3354s br, 3053m, 2927s, 1599s, 1508s, 1442s, 1367s, 1071s, 965s, 861s, 819s, 750s; δ_{H} (500MHz, CDCl_3) 1.58–1.66 (1H, m, $\text{CHH'CH}_2\text{OH}$), 1.77–1.82 (1H, m, $\text{CHH'CH}_2\text{OH}$), 2.40 (3H, br s, NH_2 & OH), 2.73 (1H, dd, $J_{13,5}$, 9Hz, ArCHH'), 3.00 (1H, dd, $J_{13,5}$, 5Hz, ArCHH'), 3.27–3.32 (1H, m, NCH), 3.82–3.91 (2H, m, CH_2OH), 7.31 (1H, dd, J_8 , 1.5Hz, aryl CH), 7.44–7.50 (2H, m, aryl CH), 7.62 (1H, s, aryl CH), 7.79–7.83 (3H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 38.07 & 46.56 (2 x CH_2), 53.98 (CH), 62.63 (CH_2), 125.72, 126.37, 127.65, 127.74, 127.85, 127.93 & 128.44 (7 x CH), 132.40, 133.68 & 136.39 (3 x quaternary); m/z (ES) 216 (MH^+ , 100%); HRMS found 216.1379, $\text{C}_{14}\text{H}_{18}\text{NO}$ (MH^+) requires 216.1388. Found: C, 77.9; H, 8.05; N, 6.3%. $\text{C}_{14}\text{H}_{17}\text{NO}$ requires C, 78.1; H, 7.95; N, 6.5%.

General Experimental Procedures (Gel-Phase):

Preparation of 11. In a septum-capped, oven-dried, round-bottomed flask containing dry beads (5.0 g, 1.04 mequiv./g, 500–560 μm polystyrene, 1–2% DVB) and CH_2Cl_2 (30 ml) was charged with TMSCl (5.1 ml, 8.0 equiv.). The beads were suspended for 15 minutes and then the solution was removed *via* a 22 gauge needle and syringe leaving the beads in the flask. The beads were washed with anhydrous CH_2Cl_2 (3 x 2 minutes each) and suspended in a solution of trifluoromethanesulfonic acid in CH_2Cl_2 (6% v/v, 44.2 ml, 6.0 equiv.) for 30 minutes, during which time the flask was carefully agitated on a wrist-action shaker. The beads turned a

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deep orange color and were drained, resuspended with CH_2Cl_2 (3 x 2 minutes each) and left suspended in the 4th volume of CH_2Cl_2 . Freshly distilled 2,6-lutidine (7.4 ml, 8.0 equiv.) and freshly distilled *cis*-oct-5-en-1-ol. (2.3 ml, 3.0 equiv.) were added and the solution was agitated at room temperature for 12 hours. The beads were then filtered, washed with CH_2Cl_2 (4 x 15 minutes each) and dried *in vacuo* to give the polymer-supported alkene (0.96 mequiv./g); ν_{max} (KBr disc)/ cm^{-1} 3082m, 3060m, 3026s, 2925s, 2863s, 1601m, 1493s, 1452s, 1101s, 882s, 757s, 698s; δ_{H} (MAS, 600MHz, CD_2Cl_2) 1.03 (br s, $\text{CH}(\text{CH}_3)_2$ and C(8) H_3), 1.42 (br s, C(3) H_2), 1.53 (br s, C(2) H_2), 2.05 (br s, C(4) H_2 and C(7) H_2), 3.66 (br s, C(1) H_2), 5.39 (br s, C(5) H and C(6) H), 6.45-7.24 (br m, aryl CH). The beads were suspended in CH_2Cl_2 (100 ml) and MeOH (3 ml); NaHCO_3 (10 mg) was added and the solution was cooled to -78°C . Ozone was bubbled through the solution for 30 minutes, followed by O_2 , in order to remove the blue color of the solution. Dimethyl sulfide (10 equiv.) was added and the resultant mixture was allowed to warm to room temperature overnight. The beads were filtered, washed with CH_2Cl_2 (4 x 15 minutes each) and dried *in vacuo* to give **11**; ν_{max} (KBr disc)/ cm^{-1} 3082m, 3060m, 3026s, 2924s, 2863s, 1725s, 1601m, 1493s, 1452s, 1101s, 882m, 757s, 698s; δ_{H} (MAS, 600MHz, CD_2Cl_2) 1.01 (br s, $\text{CH}(\text{CH}_3)_2$), 1.53 (br s, C(2) H_2), 1.66 (br s, C(3) H_2), 2.38 (br s, C(4) H_2), 3.65 (br s, C(1) H_2), 6.40-7.21 (br m, aryl CH), 9.67 (br s, C(5) H).

Reductive Amination to give 12. A glass vial, screw-capped with a Teflon-lined septum, containing the primary amino alcohol (5.5 equiv.) and the gel-phase aldehyde **11** (100 mg, *ca.* 0.96 mequiv./g) was charged with DMF and CH_2Cl_2 (1:1). The solution was agitated at room temperature for 4-18 hours, cooled to 0°C and then NaBH_4 (5.5 equiv.) was added in portions over 1 hour [Caution! Hydrogen gas evolved]. The mixture was agitated at room temperature over 24 hours. The beads were filtered, washed with CH_2Cl_2 (2 x 5 minutes each), DMF: EtOH: Et₃N (2:2:1; 2 x 5 minutes each), CH_2Cl_2 (2 x 5 minutes each), a solution of 8-hydroxyquinoline in CH_2Cl_2 (5% w/v; 4 x 15 minutes each), CH_2Cl_2 (5 x 5 minutes each) and dried *in vacuo*. In order to cleave the substrate from the polymer support, the beads were suspended in a solution of HF-pyridine in THF (5% v/v) and shaken for 3-12 hours in clear, washed Eppendorf[®] tubes, then TMSOMe (to give a 1:1 v/v solution) was added and the mixture shaken for 30 minutes. The solution was filtered through a short pad of SiO_2 and concentrated *in vacuo*.

(S)-5-(1-Benzyl-2-hydroxyethylamino)pentan-1-ol; 12a. White solid; yield: 78%; m.p. $54-56^\circ\text{C}$; R_f 0.34 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 85:10:5); ν_{max} (KBr disc)/ cm^{-1} 3346s br, 3026m, 2931s, 1602m, 1496s, 1456s, 1358m, 1120m, 1043s, 746s, 701s; δ_{H} (500MHz, CDCl_3) 1.28-1.34 (2H, m, CH_2), 1.40-1.52 (4H, m, CH_2), 2.54-2.62 (2H, m, NCH_2), 2.67 (1H, dd, J 13.5, 6.5Hz, PhCHH '), 2.76 (1H, dd, J 13.5, 7Hz, PhCHH '), 2.81-2.86 (1H, m, NCH), 2.93 (3H, br s, NH & OH), 3.32 (1H, dd, J 10.5, 6Hz, $\text{CHH}'\text{OH}$), 3.55 (2H, t, J 6.5Hz, CH_2OH), 3.56 (1H, dd, J 10.5, 4Hz, $\text{CHH}'\text{OH}$), 7.15-7.20 (3H, m, aryl CH), 7.25-7.28 (2H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 23.54, 29.92, 32.57, 38.03 & 47.15 (5 x CH_2), 60.70 (CH), 62.35 & 62.70 (2 x CH_2), 126.60, 128.77 & 129.41 (3 x CH), 138.88 (quaternary); m/z (ES) 238 (MH^+ , 100%); HRMS found 238.1798, $\text{C}_{14}\text{H}_{24}\text{NO}_2$ (MH^+) requires 238.1807. Found: C, 70.7; H, 9.85; N, 5.8%. $\text{C}_{14}\text{H}_{23}\text{NO}_2$ requires C, 70.9; H, 9.75; N, 5.9%.

(S)-5-(2-Hydroxy-1-methylethylamino)pentan-1-ol; 12b. White, waxy solid; yield: 93%; m.p. $42-44^\circ\text{C}$; R_f 0.18 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 80:15:5); ν_{max} (KBr disc)/ cm^{-1} 3298s br, 2933s, 2861s, 1457s, 1378s, 1049s, 921m, 732s; δ_{H} (500MHz, CDCl_3) 1.03 (3H, d, J 7Hz, CH_3), 1.38-1.44 (2H, m, CH_2), 1.51-1.59 (4H, m, CH_2), 2.52-2.57 (1H, m, $\text{CHH}'\text{N}$), 2.69-2.81 (2H, m, $\text{CHH}'\text{N}$ & NCH), 3.32 (1H, dd, J 10.5, 7.5Hz,

$\text{CHH}'\text{OH}$), 3.56 (1H, dd, J 10.5, 4Hz, $\text{CHH}'\text{OH}$), 3.59 (2H, t, J 6.5Hz, CH_2OH), 3.78 (3H, br s, NH & OH); δ_{C} (100MHz, CDCl_3) 16.57 (CH_3), 23.64, 29.67, 32.53 & 46.90 (4 x CH_2), 54.76 (CH), 61.99 & 65.48 (2 x CH_2); m/z (ES) 162 (MH^+ , 100%). Found: C, 59.7; H, 11.90; N, 8.6%. $\text{C}_8\text{H}_{19}\text{NO}_2$ requires C, 59.6; H, 11.90; N, 8.7%.

(S)-5-(1-Hydroxymethylpropylamino)pentan-1-ol; 12c. White solid; yield: 100%; m.p. $47-48^\circ\text{C}$; R_f 0.28 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 80:15:5); ν_{max} (KBr disc)/ cm^{-1} 3296s br, 2932s, 2861s, 1462s, 1379m, 1053s; δ_{H} (500MHz, CDCl_3) 0.91 (3H, d, J 7Hz, CH_3), 1.36-1.59 (8H, m, CH_2), 2.51-2.59 (2H, m, NCH & $\text{CHH}'\text{N}$), 2.66-2.71 (1H, m, $\text{CHH}'\text{N}$), 3.34 (1H, dd, J 10.5, 7Hz, $\text{CHH}'\text{OH}$), 3.40 (3H, br s, NH & OH), 3.59 (2H, t, J 6.5Hz, CH_2OH), 3.63 (1H, dd, J 10.5, 4Hz, $\text{CHH}'\text{OH}$); δ_{C} (100MHz, CDCl_3) 10.62 (CH_3), 23.64, 23.99, 29.95, 32.57 & 46.94 (5 x CH_2), 60.76 (CH), 62.12 & 62.71 (2 x CH_2); m/z (ES) 176 (MH^+ , 100%). Found: C, 61.6; H, 12.15; N, 7.9%. $\text{C}_9\text{H}_{21}\text{NO}_2$ requires C, 61.7; H, 12.10; N, 8.0%.

(S)-5-(1-Hydroxymethyl-2-methylpropylamino)pentan-1-ol; 12d. Colorless oil; yield: 84%; R_f 0.31 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 85:10:5); ν_{max} (thin film)/ cm^{-1} 3328s br, 2932s, 1466s, 1368m, 1054s; δ_{H} (500MHz, CDCl_3) 0.80 (3H, d, J 7Hz, CH_3), 0.86 (3H, d, J 7Hz, CH_3), 1.29-1.50 (6H, m, CH_2), 1.70-1.74 (1H, m, $\text{CH}(\text{CH}_3)_2$), 2.25-2.29 (1H, m, NCH), 2.45-2.50 (1H, m, $\text{CHH}'\text{N}$), 2.54-2.59 (1H, m, $\text{CHH}'\text{N}$), 3.07 (3H, br s, NH & OH), 3.25 (1H, dd, J 10.5, 7.5Hz, $\text{CHH}'\text{OH}$), 3.49 (2H, t, J 6.5Hz, CH_2OH), 3.50 (1H, dd, J 10.5, 4Hz, $\text{CHH}'\text{OH}$); δ_{C} (100MHz, CDCl_3) 18.47 & 19.70 (2 x CH_3), 23.63 (CH_2), 28.87 (CH), 30.23, 32.59, 47.46, 60.73 & 62.20 (5 x CH_2), 64.67 (CH); m/z (ES) 190 (MH^+ , 100%). Found: C, 63.3; H, 12.40; N, 7.3%. $\text{C}_{10}\text{H}_{23}\text{NO}_2$ requires C, 63.5; H, 12.25; N, 7.4%.

(S)-2-(5-Hydroxypentylamino)-4-methylpentan-1-ol; 12e. White, waxy solid; yield: 94%; m.p. $42-44^\circ\text{C}$; R_f 0.21 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 85:10:5); ν_{max} (KBr disc)/ cm^{-1} 3310s br, 2930s, 1466s, 1367m, 1056s; δ_{H} (500MHz, CDCl_3) 0.82 (6H, d, J 6.5Hz, CH_3), 1.10-1.15 (1H, m, $\text{CHH}'\text{CH}(\text{CH}_3)_2$), 1.20-1.25 (1H, m, $\text{CHH}'\text{CH}(\text{CH}_3)_2$), 1.29-1.35 (2H, m, CH_2), 1.40-1.56 (5H, m, CH_2 & $\text{CH}(\text{CH}_3)_2$), 2.47 (1H, dt, J 11, 7Hz, $\text{CHH}'\text{N}$), 2.53-2.60 (2H, m, NCH & $\text{CHH}'\text{N}$), 3.20 (1H, dd, J 10.5, 7Hz, $\text{CHH}'\text{OH}$), 3.26 (3H, br s, NH & OH), 3.50 (2H, t, J 6.5Hz, CH_2OH), 3.52 (1H, dd, J 10.5, 3.5Hz, $\text{CHH}'\text{OH}$); δ_{C} (100MHz, CDCl_3) 22.75 & 23.41 (2 x CH_3), 23.66 (CH_2), 25.20 (CH), 30.07, 32.59, 40.89 & 46.97 (4 x CH_2), 57.24 (CH), 62.06 & 63.40 (2 x CH_2); m/z (ES) 204 (MH^+ , 100%). Found: C, 64.9; H, 12.50; N, 6.7%. $\text{C}_{11}\text{H}_{25}\text{NO}_2$ requires C, 65.0; H, 12.40; N, 6.9%.

(S)-5-(2-Hydroxy-1-phenylethylamino)pentan-1-ol; 12f. Colorless oil; yield: 92%; R_f 0.33 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 85:10:5); ν_{max} (thin film)/ cm^{-1} 3326s br, 2932s, 2859s, 1454s, 1353m, 1063s, 759s, 702s; δ_{H} (500MHz, CDCl_3) 1.31-1.36 (2H, m, CH_2), 1.44-1.52 (4H, m, CH_2), 2.40-2.50 (2H, m, NCH_2), 3.53 (2H, t, J 6.5Hz, CH_2OH), 3.54 (1H, dd, J 10.5, 7.5Hz, $\text{CHH}'\text{OH}$), 3.65 (1H, dd, J 10.5, 4Hz, $\text{CHH}'\text{OH}$), 3.73 (1H, dd, J 9, 4Hz, NCH), 7.21-7.31 (5H, m, aryl CH); δ_{C} (100MHz, CDCl_3) 23.63, 29.77, 32.59, 47.51 & 62.20 (5 x CH_2), 65.07 (CH), 66.79 (CH_2), 127.61, 127.76 & 128.78 (3 x CH), 140.66 (quaternary); m/z (ES) 224 (MH^+ , 100%). Found: C, 69.8; H, 9.60; N, 6.1%. $\text{C}_{13}\text{H}_{21}\text{NO}_2$ requires C, 69.9; H, 9.50; N, 6.3%.

(S,S)-5-(2-Hydroxy-1-methoxymethyl-2-phenylethylamino)pentan-1-ol; 12g. White solid; yield: 90%; m.p. $75-78^\circ\text{C}$; R_f 0.43 (base-washed SiO_2 ; EtOAc: MeOH: Et₃N; 90:5:5); ν_{max} (KBr disc)/ cm^{-1} 3359s br, 2931s, 1454s, 1194m, 1109s, 1048s, 702s; δ_{H} (500MHz, CDCl_3) 1.27-1.33 (2H,

m, CH_2), 1.39-1.49 (4H, m, CH_2), 2.37-2.42 (1H, m, $\text{CHH}'\text{N}$), 2.59-2.68 (2H, m, $\text{CHH}'\text{N}$ & NCH), 3.05 (1H, dd, J10, 4.5Hz, $\text{CHH}'\text{OMe}$), 3.22, (3H, s, OCH_3), 3.33 (1H, dd, J10, 3.5Hz, $\text{CHH}'\text{OMe}$), 3.49 (2H, t, J6.5Hz, CH_2OH), 4.42 (1H, d, J8Hz, CHOH), 7.19-7.31 (5H, m, aryl CH); δ_c (100MHz, CDCl_3) 23.53, 30.30, 32.62 & 47.75 (4 x CH_2), 59.18 (CH_3), 62.39 (CH_2), 64.48 (CH), 70.21 (CH_2), 72.77, 126.92, 127.69 & 128.43 (4 x CH), 142.44 (quaternary); m/z (ES) 268 (MH^+ , 100%). Found: C, 67.3; H, 9.55; N, 5.2%. $\text{C}_{15}\text{H}_{25}\text{NO}_3$ requires C, 67.4; H, 9.40; N, 5.2%.

(S)-5-(2-Cyclohexyl-1-

hydroxymethylethylamino)pentan-1-ol; 12h. White solid; yield: 99%; m.p. 39-40°C; R_f 0.36 (base-washed SiO_2 ; EtOAc: MeOH: Et_3N ; 80:15:5); ν_{max} (KBr disc)/ cm^{-1} 3335s br, 2922s, 2851s, 1448s, 1055s; δ_H (500MHz, CDCl_3) 0.88-1.74 (19H, m), 2.57 (1H, dt, J13.5, 7Hz, $\text{CHH}'\text{N}$), 2.66-2.73 (2H, m, $\text{CHH}'\text{N}$ & NCH), 3.17 (3H, br s, NH & OH), 3.28 (1H, dd, J10.5, 7Hz, $\text{CHH}'\text{OH}$), 3.61 (2H, t, J6.5Hz, CH_2OH), 3.63 (1H, dd, J10.5, 3.5Hz, $\text{CHH}'\text{OH}$); δ_c (100MHz, CDCl_3) 23.62, 26.41, 26.45, 26.70, 29.93, 32.56, 33.58 & 34.11 (8 x CH_2), 34.75 (CH), 39.36 & 46.84 (2 x CH_2), 56.60 (CH), 62.31 & 63.35 (2 x CH_2); m/z (ES) 244 (MH^+ , 100%). Found: C, 69.0; H, 12.00; N, 5.7%. $\text{C}_{14}\text{H}_{29}\text{NO}_2$ requires C, 69.1; H, 12.00; N, 5.8%.

(S)-5-[1-(2-Bromophenoxyethyl)-2-

phenylethylamino]pentan-1-ol; 12i. Colorless oil; yield: 97%; R_f 0.22 (base-washed SiO_2 ; Hexane: EtOAc: Et_3N ; 30:65:5); ν_{max} (thin film)/ cm^{-1} 3364m br, 2928s, 2855m, 1586m, 1481s, 1277s, 1248s, 1052s, 1030s, 746s, 700s; δ_H (500MHz, CDCl_3) 1.35-1.42 (2H, m, CH_2), 1.49-1.58 (4H, m, CH_2), 1.60 (2H, br s, NH & OH), 2.74 (2H, t, J7Hz, NCH_2), 2.94 (2H, d, J7Hz, PhCH_2), 2.96-3.23 (1H, m, NCH), 3.62 (CH_2 , t, J6.5Hz, CH_2OH), 3.87 (1H, dd, J9, 5.5Hz, $\text{CHH}'\text{OAr}$), 3.92 (1H, dd, J9, 5Hz, $\text{CHH}'\text{OAr}$), 6.80 (1H, dd, J8.5, 1Hz, aryl CH), 6.83 (1H, td, J8, 1.5Hz, aryl CH), 7.20-7.31 (6H, m, aryl CH), 7.54 (1H, dd, J8, 1.5Hz, aryl CH); δ_c (100MHz, CDCl_3) 23.52, 30.12, 32.70, 38.20 & 47.53 (5 x CH_2), 58.73 (CH), 63.01 & 69.95 (2 x CH_2), 112.51 (quaternary), 113.45, 122.19, 126.59, 128.70, 128.76, 129.56 & 133.49 (7 x CH), 138.91 & 155.27 (2 x quaternary); m/z (ES) 392 (MH^+ , ^{79}Br , 100%), 394 (MH^+ , ^{81}Br , 84%); HRMS found 392.1217, $\text{C}_{20}\text{H}_{27}\text{BrNO}_2$ (MH^+ , ^{79}Br) requires 392.1225. Found: C, 61.1; H, 6.95; Br, 20.4; N, 3.5%. $\text{C}_{20}\text{H}_{26}\text{BrNO}_2$ requires C, 61.2; H, 6.70; Br, 20.4; N, 3.6%.

(S)-5-(3-Hydroxy-1-naphthalen-2-

ylmethylpropylamino)pentan-1-ol; 12j. Colorless oil; yield: 92%; R_f 0.26 (base-washed SiO_2 ; EtOAc: MeOH: Et_3N ; 85:10:5); ν_{max} (thin film)/ cm^{-1} 3293s br, 2930s, 2857s, 1600m, 1508s, 1456s, 1367s, 1057s, 857m, 819s, 750s; δ_H (500MHz, CDCl_3) 1.31-1.36 (2H, m, CH_2), 1.42-1.59 (5H, m, CH_2 & $\text{CHH}'\text{CH}_2\text{OH}$), 1.74-1.79 (1H, m, $\text{CHH}'\text{CH}_2\text{OH}$), 2.67-2.78 (2H, m, NCH_2), 2.82 (1H, dd, J13, 7Hz, ArCHH'), 3.08 (1H, dd, J13, 6Hz, ArCHH'), 3.11-3.16 (1H, m, NCH), 3.40 (3H, br s, NH_2 & OH), 3.54 (2H, t, J6.5Hz, CH_2OH), 3.60-3.76 (1H, m, $\text{CHH}'\text{OH}$), 3.85-3.89 (1H, m, $\text{CHH}'\text{OH}$), 7.28 (1H, dd, J8.5, 1.5Hz, aryl CH), 7.42-7.49 (2H, m, aryl CH), 7.59 (1H, s, aryl CH), 7.77-7.82 (3H, m, aryl CH); δ_c (100MHz, CDCl_3) 23.52, 29.82, 32.58, 33.60, 40.54 & 46.65 (6 x CH_2), 60.60 (CH), 62.53 & 62.72 (2 x CH_2), 125.81, 126.45, 127.66, 127.74, 127.89, 127.94 & 128.51 (7 x CH), 132.42, 133.73 & 136.20 (3 x quaternary); m/z (ES) 302 (MH^+ , 100%). Found: C, 75.6; H, 9.20; N, 4.5%. $\text{C}_{19}\text{H}_{27}\text{NO}_2$ requires C, 75.7; H, 9.05; N, 4.7%.

Reductive Alkylation to give 13. A glass vial, screw-capped with a Teflon-lined septum, containing the polymer-supported secondary amine **12a** (100 mg, 0.70 mequiv./g), MeOH (2 ml) and CH_2Cl_2 (0.5 ml) was charged with benzaldehyde (10

equiv.) and then borane-pyridine (10 equiv., 8M, solution in excess pyridine). The solution was agitated at room temperature for 4 days. The beads were filtered, washed with MeOH: CH_2Cl_2 (1:1; 3 x 5 minutes each), DMF: EtOH: Et_3N (2:2:1; 3 x 5 minutes each), CH_2Cl_2 (2 x 5 minutes each), a solution of 8-hydroxyquinoline in CH_2Cl_2 (5% w/v; 4 x 15 minutes each), CH_2Cl_2 (5 x 5 minutes each) and dried *in vacuo*. In order to cleave the substrate from the polymer-support, the beads were suspended in a solution of HF-pyridine in THF (5% v/v) and shaken for 1.5 hours in a clear, washed Eppendorf® tube, then TMSOMe (to give a 1:1 v/v solution) was added and the mixture shaken for 30 minutes. The solution was filtered through a short pad of SiO_2 and concentrated *in vacuo*.

(S)-5-[(1-Benzyl-2-hydroxyethyl)-(2-bromobenzyl)-amino]-pentan-1-ol; 13aa. Colorless oil; yield: 97%; R_f 0.22 (SiO_2 ; Hexane: EtOAc: 1:1); ν_{max} (thin film)/ cm^{-1} 3389s br, 3062m, 2936s, 2862s, 1602m, 1567m, 1495m, 1456s, 1246m, 1130s, 1028s, 910s, 733s, 700s; δ_H (500MHz, CDCl_3) 1.24-1.42 (2H, m, CH_2), 1.45-1.56 (4H, m, CH_2), 2.03 (1H, br s, OH), 2.40 (1H, dd, J13, 10Hz, PhCHH'), 2.49-2.54 (1H, m, NCHH'), 2.64-2.70 (1H, m, NCHH'), 2.97-3.03 (1H, m, NCH), 3.06 (1H, dd, J13, 4.5Hz, PhCHH'), 3.20 (1H, br s, OH), 3.31 (1H, dd, J10.5, 4.5Hz, $\text{CHH}'\text{OH}$), 3.40 (1H, dd, J10.5, 10.5Hz, $\text{CHH}'\text{OH}$), 3.56 (2H, t, J6.5Hz, CH_2OH), 3.77 (1H, d, J14Hz, ArCHH'), 3.91 (1H, d, J14Hz, ArCHH'), 7.10-7.20 (4H, m, aryl CH), 7.22-7.29 (3H, m, aryl CH), 7.34 (1H, dd, J8, 1.5Hz, aryl CH), 7.54 (1H, dd, J8.5, 1Hz, aryl CH); δ_c (100MHz, CDCl_3) 23.76, 28.66, 32.11, 32.68, 49.28, 54.55, 60.80 & 62.81 (8 x CH_2), 62.96 (CH), 124.82 (quaternary), 126.46, 127.72, 128.78, 129.09, 129.24, 131.53 & 133.33 (7 x CH), 138.48 & 139.38 (2 x quaternary); m/z (ES) 406 (MH^+ , ^{79}Br , 100%), 408 (MH^+ , ^{81}Br , 94%); HRMS found 406.1398, $\text{C}_{21}\text{H}_{29}\text{BrNO}_2$ (MH^+ , ^{79}Br) requires 406.1381. Found: C, 62.1; H, 7.05; Br, 19.3; N, 3.5%. $\text{C}_{21}\text{H}_{28}\text{BrNO}_2$ requires C, 62.1; H, 6.95; Br, 19.7; N, 3.5%.

(S)-5-[(2-Bromo-5-chlorobenzyl)-(1-hydroxymethyl-2-phenylethyl)-amino]-pentan-1-ol; 13ab. Colorless oil; yield: 92%; R_f 0.30 (SiO_2 ; Hexane: EtOAc: 1:1); ν_{max} (thin film)/ cm^{-1} 3373s br, 3061m, 3025m, 2934s, 2859s, 1495m, 1454s, 1381m, 1238m, 1189s, 1131m, 1026s, 810m, 744s, 700s; δ_H (500MHz, CDCl_3) 1.28-1.42 (2H, m, CH_2), 1.48-1.56 (4H, m, CH_2), 1.78 (1H, br s, OH), 2.42 (1H, dd, J13, 10Hz, PhCHH'), 2.51-2.56 (1H, m, NCHH'), 2.63-2.69 (1H, m, NCHH'), 2.97-3.04 (3H, m, OH , NCH & PhCHH'), 3.36 (1H, dd, J11, 5Hz, $\text{CHH}'\text{OH}$), 3.43 (1H, dd, J10.5, 10.5Hz, $\text{CHH}'\text{OH}$), 3.60 (2H, t, J6.5Hz, CH_2OH), 3.70 (1H, d, J14Hz, ArCHH'), 3.86 (1H, d, J14Hz, ArCHH'), 7.08-7.31 (7H, m, aryl CH), 7.46 (1H, d, J9Hz, aryl CH); δ_c (100MHz, CDCl_3) 23.76, 28.61, 32.32, 32.65, 49.49, 54.50, 60.99 & 62.86 (8 x CH_2), 63.14 (CH), 122.37 (quaternary), 126.57, 128.86, 129.10, 129.24 & 131.27 (5 x CH), 133.77 (quaternary), 134.28 (CH), 139.30 & 140.42 (2 x quaternary); m/z (ES) 440 (MH^+ , ^{79}Br ^{35}Cl , 90%), 442 (MH^+ , 100%), 444 (MH^+ , 15%); HRMS found 440.0880, $\text{C}_{21}\text{H}_{28}\text{BrClNO}_2$ (MH^+ , ^{79}Br ^{35}Cl) requires 440.0914.

(S)-5-[(2-Bromo-5-methoxybenzyl)-(1-hydroxymethyl-2-phenylethyl)-amino]-pentan-1-ol; 13ac. Colorless oil; yield: 91%; R_f 0.33 (SiO_2 ; Hexane: EtOAc: 1:2); ν_{max} (thin film)/ cm^{-1} 3387s br, 3024m, 2935s, 2858s, 1593m, 1495m, 1464s, 1267m, 1160m, 1126m, 1018s, 810m, 743s, 700s; δ_H (500MHz, CDCl_3) 1.30-1.43 (2H, m, CH_2), 1.48-1.57 (4H, m, CH_2), 1.98 (1H, br s, OH), 2.41 (1H, dd, J13, 10Hz, PhCHH'), 2.50-2.55 (1H, m, NCHH'), 2.65-2.71 (1H, m, NCHH'), 3.00-3.07 (2H, m, NCH & PhCHH'), 3.15 (1H, br s, OH), 3.33 (1H, dd, J10.5, 4.5Hz, $\text{CHH}'\text{OH}$), 3.41 (1H, dd, J10.5, 10.5Hz, $\text{CHH}'\text{OH}$), 3.57 (2H, t, J6.5Hz, CH_2OH), 3.72 (1H, d, J14Hz, ArCHH'), 3.76 (3H, s, CH_3), 3.85 (1H, d, J14Hz, ArCHH'), 6.68

(1H, dd, *J*₉, 3Hz, aryl CH), 6.95 (1H, d, *J*₃Hz, aryl CH), 7.13-7.28 (5H, m, aryl CH), 7.42 (1H, d, *J*_{8.5}Hz, aryl CH); δ_c (100MHz, CDCl₃) 23.77, 28.61, 32.15, 32.69, 49.33 & 54.54 (6 x CH₂), 55.70 (CH₃), 60.84 & 62.82 (2 x CH₂), 62.91 & 114.79 (2 x CH), 114.99 (quaternary), 116.86, 126.46, 128.79, 129.25 & 133.78 (5 x CH), 139.42, 139.51 & 159.25 (3 x quaternary); *m/z* (ES) 436 (MH⁺, ⁷⁹Br, 100%), 438 (MH⁺, ⁸¹Br, 96%); HRMS found 436.1403, C₂₂H₃₁BrNO₃ (MH⁺, ⁷⁹Br) requires 436.1409.

(S)-5-[(2-Bromo-4,5-dimethoxybenzyl)-(1-hydroxymethyl-2-phenylethyl)-amino]-pentan-1-ol; 13ad. Colorless oil; yield: 81%; *R*_f 0.26 (SiO₂; Hexane: EtOAc; 1:4); ν_{max} (thin film)/cm⁻¹ 3404s br, 3024m, 2934s, 2857m, 1601m, 1504s, 1455m, 1438m, 1381m, 1257s, 1209s, 1156m, 1031s, 801m, 743m, 700s; δ_H (500MHz, CDCl₃) 1.30-1.46 (2H, m, CH₂), 1.50-1.59 (4H, m, CH₂), 2.41 (1H, dd, *J*₁₃, 10Hz, PhCHH'), 2.50-2.55 (1H, m, NCHH'), 2.66-2.72 (1H, m, NCHH'), 2.98-3.03 (1H, m, NCH), 3.06 (1H, dd, *J*₁₃, 4Hz, PhCHH'), 3.33 (1H, dd, *J*_{10.5}, 5Hz, CHH'OH), 3.41 (1H, dd, *J*_{10.5}, 10.5Hz, CHH'OH), 3.59 (2H, t, *J*_{6.5}Hz, CH₂OH), 3.72 (1H, d, *J*_{13.5}Hz, ArCHH'), 3.83 (3H, s, CH₃), 3.84 (1H, d, *J*_{13.5}Hz, ArCHH'), 3.85 (3H, s, CH₃), 6.86 (1H, s, aryl CH), 7.01 (1H, s, aryl CH), 7.14-7.28 (5H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.81, 28.62, 32.12, 32.67, 48.98 & 54.04 (6 x CH₂), 56.28 & 56.37 (2 x CH₃), 60.76 (CH₂), 62.50 (CH), 62.84 (CH₂), 113.91 (CH), 114.61 (quaternary), 115.79, 126.46, 128.78 & 129.21 (4 x CH), 130.28, 139.43, 148.68 & 148.95 (4 x quaternary); *m/z* (ES) 466 (MH⁺, ⁷⁹Br, 100%), 468 (MH⁺, ⁸¹Br, 80%); HRMS found 466.1528, C₂₃H₃₃BrNO₄ (MH⁺, ⁷⁹Br) requires 466.1515.

Alkylation of Polymer-Supported Alcohols. An oven-dried, glass vial, screw-capped with a Teflon-lined septum, containing the polymer-supported alcohol **13** (100 mg) suspended in anhydrous THF (4 ml) was charged with a solution of KHMDS in THF (1M, 12.5 equiv.). The solution was agitated at room temperature for 10 hours. The beads turned an orange-brown color, depending on the substrate, and were drained and washed with THF (3 x 2 minutes each). The benzyl bromide (25 equiv.) was added as a solution in anhydrous THF (5 ml) and the mixture agitated at room temperature. The beads returned to their original color as the reaction proceeded. After 14 hours the beads were drained³⁶ and washed with THF (3 x 5 minutes each). The treatment with KHMDS followed by the benzyl bromide was repeated at this stage. The beads were filtered, washed with MeOH: CH₂Cl₂ (1:1; 3 x 5 minutes each), CH₂Cl₂ (2 x 5 minutes each), a solution of 8-hydroxyquinoline (5% w/v) in MeOH and CH₂Cl₂ (1:1; 4 x 30 minutes each), CH₂Cl₂ (5 x 5 minutes each) and dried *in vacuo*. In order to cleave the substrate from the polymer-support, the beads were suspended in a solution of HF-pyridine in THF (5% v/v) and shaken for 1.5 hours in a clear, washed Eppendorf® tube, then TMSOMe (to give a 1:1 v/v solution) was added and the mixture shaken for 30 minutes. The solution was filtered through a short pad of SiO₂ and concentrated *in vacuo*.

(S)-5-[[1-Benzyl-2-(2-bromobenzyloxy)ethyl]-(2-bromobenzyl)-amino]-pentan-1-ol; 14aaa. Colorless oil; yield: 88%; *R*_f 0.12 (SiO₂; Hexane: EtOAc; 4:1); ν_{max} (thin film)/cm⁻¹ 3348s br, 3061m, 3025m, 2932s, 2858s, 1568m, 1495m, 1466s, 1440s, 1357s, 1127s, 1044s, 1026s, 750s, 700s; δ_H (500MHz, CDCl₃) 1.24-1.33 (2H, m, CH₂), 1.35-1.49 (4H, m, CH₂), 2.61-2.71 (2H, m, NCH₂), 2.84 (1H, dd, *J*_{13.5}, 8Hz, PhCHH'), 2.89 (1H, dd, *J*₁₃, 6.5Hz, PhCHH'), 3.13-3.18 (1H, m NCH), 3.54 (2H, t, *J*_{6.5}Hz, CH₂OH), 3.60 (1H, dd, *J*₁₀, 5Hz, CHH'OCH₂Ar), 3.68 (1H, dd, *J*₁₀, 6.5Hz, CHH'OCH₂Ar), 3.85-3.93 (2H, ABq, *J*₁₇Hz, NCH₂Ar), 4.50 (2H, s, OCH₂Ar), 7.01-7.52 (13H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.60, 28.82, 32.88,

35.28, 50.97 & 55.39 (6 x CH₂), 62.15 (CH), 63.16, 71.08 & 72.69 (3 x CH₂), 122.50 & 123.88 (2 x quaternary), 126.11, 127.34, 127.59, 128.07, 128.49, 129.04, 129.64, 130.60, 132.47 & 132.58 (11 x CH), 138.13, 140.26 & 140.63 (3 x quaternary); *m/z* (ES) 574 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 576 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 578 (MH⁺, ⁸¹Br ⁸¹Br, 48%); HRMS found 574.0938, C₂₈H₃₄Br₂NO₂ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 574.0956. Found: C, 58.5; H, 5.70; Br, 27.8; N, 2.8%. C₂₈H₃₃Br₂NO₂ requires C, 58.5; H, 5.80; Br, 27.8; N, 2.4%.

(R)-5-[(2-Bromobenzyl)-[2-(2-bromo-4-fluorobenzyloxy)-1-phenylethyl]-amino]-pentan-1-ol; 14fab. Colorless oil; yield: 69%; *R*_f 0.43 (SiO₂; Hexane: EtOAc; 2:1); ν_{max} (thin film)/cm⁻¹ 3382m br, 3061m, 2933s, 2859s, 1599s, 1487s, 1230s, 1106s, 1026s, 752s, 701s; δ_H (500MHz, CDCl₃) 1.22-1.50 (6H, m, CH₂), 2.42-2.47 (1H, m, NCHH'), 2.59-2.65 (1H, m, NCHH'), 3.53-3.56 (2H, br m, CH₂OH), 3.74-3.86 (2H, ABq, *J*_{15.5}Hz, NCH₂Ar), 3.89 (1H, dd, *J*_{9.5}, 6Hz, PhCH), 4.02-4.09 (2H, m, CH₂OCH₂Ar), 4.48-4.54 (2H, ABq, *J*₁₃Hz, OCH₂Ar), 6.97 (1H, td, *J*_{8.5}, 2.5Hz, aryl CH), 7.08 (1H, td, *J*₈, 2Hz, aryl CH), 7.25-7.38 (8H, m, aryl CH), 7.49 (1H, dd, *J*₈, 1Hz, aryl CH), 7.69 (1H, dd, *J*₈, 1.5Hz, aryl CH); δ_c (100MHz, CDCl₃) 23.60, 27.70, 32.76, 51.09, 55.15 & 63.06 (6 x CH₂), 63.87 (CH), 71.69 & 72.02 (2 x CH₂), 114.66 (d, *J*_{20.5}Hz, CH), 119.83 (d, *J*₂₅Hz, CH), 122.56 (d, *J*_{9.5}Hz, quaternary), 124.00 (quaternary), 127.44, 127.45, 128.29, 128.41 & 128.81 (5 x CH), 130.23 (d, *J*₈Hz, CH), 130.69 & 132.73 (2 x CH), 133.84 (d, *J*₃Hz, quaternary), 139.80 & 140.04 (2 x quaternary), 161.85 (d, *J*_{249.5}Hz, quaternary); *m/z* (ES) 578 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 580 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 582 (MH⁺, ⁸¹Br ⁸¹Br, 40%); HRMS found 578.0688, C₂₇H₃₁Br₂FNO₂ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 578.0705. Found: C, 56.0; H, 5.40; Br, 27.6; F, 3.2; N, 2.4%. C₂₇H₃₀Br₂FNO₂ requires C, 56.0; H, 5.20; Br, 27.6; F, 3.3; N, 2.4%.

(R)-5-[(2-Bromobenzyl)-[2-(1-bromonaphthalen-2-ylmethoxy)-1-phenylethyl]-amino]-pentan-1-ol; 14fac. Colorless oil; yield: 72%; *R*_f 0.38 (SiO₂; Hexane: EtOAc; 2:1); ν_{max} (thin film)/cm⁻¹ 3363m br, 3059m, 2932s, 2859s, 1599w, 1502m, 1464s, 1439s, 1326s, 1257m, 1116s, 1025s, 967m, 814s, 752s, 702s; δ_H (500MHz, CDCl₃) 1.21-1.50 (6H, m, CH₂), 2.42-2.47 (1H, m, NCHH'), 2.61-2.67 (1H, m, NCHH'), 3.50-3.54 (2H, br m, CH₂OH), 3.75-3.87 (2H, ABq, *J*_{15.5}Hz, NCH₂Ar), 3.95 (1H, dd, *J*_{9.5}, 6Hz, PhCH), 4.07-4.14 (2H, m, CH₂OCH₂Ar), 4.79-4.85 (2H, ABq, *J*_{13.5}Hz, OCH₂Ar), 7.06 (1H, td, *J*₈, 1.5Hz, aryl CH), 7.23-7.60 (10H, m, aryl CH), 7.70 (1H, dd, *J*₈, 1.5Hz, aryl CH), 7.76 (1H, d, *J*_{8.5}Hz, aryl CH), 7.82 (1H, d, *J*₈Hz, aryl CH), 8.30 (1H, d, *J*₈Hz, aryl CH); δ_c (100MHz, CDCl₃) 23.60, 27.72, 32.78, 51.05, 55.16 & 63.09 (6 x CH₂), 63.88 (CH), 71.64 & 73.42 (2 x CH₂), 122.46 & 124.03 (2 x quaternary), 126.23, 126.67, 127.23, 127.45, 127.46, 127.62, 127.89, 128.28, 128.40, 128.42, 128.88 & 130.76 (12 x CH), 132.34 (quaternary), 132.71 (CH), 134.21, 136.17, 139.86 & 140.07 (4 x quaternary); *m/z* (ES) 610 (MH⁺, ⁷⁹Br ⁷⁹Br, 50%), 612 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 614 (MH⁺, ⁷⁹Br ⁸¹Br, 45%); HRMS found 610.0978, C₃₁H₃₄Br₂NO₂ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 610.0956. Found: C, 60.8; H, 5.35; N, 2.0%. C₃₁H₃₃Br₂NO₂ requires C, 60.9; H, 5.45; N, 2.3%.

(R)-5-[[2-(6-Bromobenzo[1,3]dioxol-5-ylmethoxy)-1-phenylethyl]-(2-bromo-4,5-dimethoxybenzyl)-amino]-pentan-1-ol; 14fdd. Colorless oil; yield: 53%; *R*_f 0.28 (SiO₂; Hexane: EtOAc; 1:1); ν_{max} (thin film)/cm⁻¹ 3398m br, 2933s, 1602w, 1502s, 1478s, 1381m, 1248s, 1208m, 1154m, 1113m, 1036s, 702m; δ_H (500MHz, CDCl₃) 1.26-1.53 (6H, m, CH₂), 2.42-2.47 (1H, m, NCHH'), 2.63-2.69 (1H, m, NCHH'), 3.56 (2H, t, *J*_{6.5}Hz, CH₂OH), 3.64 (1H, d, *J*₁₅Hz, NCHH'Ar), 3.76 (1H, d, *J*₁₅Hz, NCHH'Ar), 3.77 (3H, s,

(36) The excess benzyl bromide was recycled after chromatography.

OCH₃), 3.85 (3H, s, OCH₃), 3.86 (1H, dd, *J*9.5, 6Hz, PhCH), 4.01-4.09 (2H, m, CH₂OCH₂Ar), 4.46-4.51 (2H, ABq, *J*13Hz, OCH₂Ar), 5.96 (2H, s, OCH₂O), 6.89 (1H, s, aryl CH), 6.95 (1H, s, aryl CH), 6.97 (1H, s, aryl CH), 7.24 (1H, s, aryl CH), 7.25-7.36 (5H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.71, 27.91, 32.81, 50.78 & 54.31 (5 x CH₂), 56.05 & 56.38 (2 x CH₃), 63.11 (CH₂), 63.42 (CH), 71.08, 72.54 & 101.92 (3 x CH₃), 109.31 & 112.68 (2 x CH), 113.13 (quaternary), 113.25 (CH), 113.30 (quaternary), 115.27, 127.423, 128.35 & 128.78 (4 x CH), 131.10, 132.04, 139.67, 147.63, 147.82, 148.31 & 148.56 (7 x quaternary); *m/z* (ES) 664 (MH⁺, ⁷⁹Br ⁷⁹Br, 60%), 666 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 668 (MH⁺, ⁸¹Br ⁸¹Br, 58%); HRMS found 664.0932, C₃₀H₃₆Br₂NO₆ (MH⁺, ⁷⁹Br ⁷⁹Br) requires 664.0909. Found: C, 54.2; H, 5.35; Br, 24.0; N, 1.9%. C₃₀H₃₅Br₂NO₆ requires C, 54.2; H, 5.30; Br, 24.0; N, 2.1%.

(R)-5-[(2-Bromobenzyl)-[2-(4-bromothiophen-3-ylmethoxy)-1-phenylethyl]-amino]-pentan-1-ol; 14fae. Colorless oil; yield: 67%; *R_f* 0.38 (SiO₂; Hexane: EtOAc; 2:1); ν_{max} (thin film)/cm⁻¹ 3396m br, 2932s, 2859s, 1439s, 1358m, 1086s, 1025s, 985s, 793s, 751s, 701s; δ_H (500MHz, CDCl₃) 1.22-1.49 (6H, m, CH₂), 2.41-2.46 (1H, m, NCHH'), 2.59-2.64 (1H, m, NCHH'), 3.53-3.55 (2H, m, CH₂OH), 3.73-3.85 (2H, ABq, *J*15.5Hz, NCH₂Ar), 3.88 (1H, dd, *J*9.5, 6Hz, PhCH), 4.00-4.07 (2H, m, CH₂OCH₂Ar), 4.42-4.48 (2H, ABq, *J*12.5Hz, OCH₂Ar), 7.08 (1H, td, *J*8, 2Hz, aryl CH), 7.16 (1H, dt, *J*3.5, 1Hz, aryl CH), 7.23-7.37 (7H, m, aryl CH), 7.49 (1H, dd, *J*8, 1Hz, aryl CH), 7.68 (1H, dd, *J*8, 1.5Hz, aryl CH); δ_c (100MHz, CDCl₃) 23.58, 27.69, 32.76, 51.03, 55.11 & 63.09 (6 x CH₂), 63.76 (CH), 68.39 & 71.50 (2 x CH₂), 110.83 (quaternary), 123.53 & 124.00 (2 x CH), 124.03 (quaternary), 127.40, 127.45, 128.28, 128.38, 128.82, 130.77 & 132.71 (7 x CH), 138.05, 139.88 & 140.07 (3 x quaternary); *m/z* (ES) 566 (MH⁺, ⁷⁹Br ⁷⁹Br, 60%), 568 (MH⁺, ⁷⁹Br ⁸¹Br, 100%), 570 (MH⁺, ⁸¹Br ⁸¹Br, 50%); HRMS found 566.0337, C₂₅H₃₀Br₂NO₂S (MH⁺, ⁷⁹Br ⁷⁹Br) requires 566.0364. Found: C, 53.1; H, 5.05; N, 2.4; S, 5.5%. C₂₅H₂₉Br₂NO₂S requires C, 52.9; H, 5.15; N, 2.5; S, 5.7%.

(R)-5-[[2-(2-Bromo-5-chlorobenzo[*b*]thiophen-3-ylmethoxy)-1-phenylethyl]-(2-bromo-4,5-dimethoxybenzyl)-amino]-pentan-1-ol; 14fdf. Colorless oil; yield: 63%; *R_f* 0.36 (SiO₂; Hexane: EtOAc; 1:1); ν_{max} (thin film)/cm⁻¹ 3441m br, 2932s, 2858s, 1601w, 1502s, 1435s, 1380m, 1255s, 1208s, 1154s, 1112s, 1078s, 1032m, 800m, 702m; δ_H (500MHz, CDCl₃) 1.20-1.46 (6H, m, CH₂), 2.35-2.41 (1H, m, NCHH'), 2.54-2.60 (1H, m, NCHH'), 3.53 (2H, t, *J*6.5Hz, CH₂OH), 3.56-3.71 (2H, ABq, *J*15.5Hz, NCH₂Ar), 3.72 (3H, s, CH₃), 3.83 (1H, dd, *J*9.5, 6.5Hz, PhCH), 3.84 (3H, s, CH₃), 3.94-4.01 (2H, m, CH₂OCH₂Ar), 4.66-4.72 (2H, ABq, *J*12Hz, OCH₂Ar), 6.93 (1H, s, aryl CH), 7.13 (1H, s, aryl CH), 7.23-7.31 (6H, m, aryl CH), 7.61-7.49 (1H, d, *J*8.5Hz, aryl CH), 7.71 (1H, d, *J*2Hz, aryl CH); δ_c (100MHz, CDCl₃) 23.63, 27.87, 32.74, 50.83 & 54.28 (5 x CH₂), 55.95 & 56.36 (2 x CH₃), 63.07 (CH₂), 63.35 (CH), 65.65 & 70.52 (2 x CH₂), 113.19 (CH), 113.33 (quaternary), 115.26 (CH), 118.29 (quaternary), 122.36, 122.75, 125.55, 127.47, 128.33 & 128.75 (6 x CH), 131.44, 131.83, 131.91, 137.87, 139.31, 139.41, 148.31 & 148.49 (8 x quaternary); *m/z* (ES) 710 (MH⁺, ⁷⁹Br ⁷⁹Br ³⁵Cl, 40%), 712 (MH⁺, 100%), 714 (MH⁺, 62%); HRMS found 710.0346, C₃₁H₃₅Br₂ClNO₄S (MH⁺, ⁷⁹Br ⁷⁹Br ³⁵Cl) requires 710.0342.

Biaryl Synthesis. An oven-dried, glass vial, screw-capped with a Teflon-lined septum, containing the polymer-supported cyclization precursor **14** (100 mg)³⁷ in anhydrous 2-MeTHF (2 ml) was cooled to 0°C and charged with a preformed

solution of *i*-PrBu₂MgLi (5.0 equiv.).³⁸ The mixture was agitated for 6 hours at 0°C.³⁹ A freshly prepared solution of CuCN·2LiBr in 2-MeTHF (1M, 5.0 equiv.) was added and the mixture was agitated for 6 hours at 0°C. A freshly prepared solution of 1,3-dinitrobenzene in 2-MeTHF (1M, 20 equiv.) was added to give a dark brown-black solution, which was agitated for 12 hours at 0°C. The beads were filtered, washed with THF (3 x 5 minutes each), MeOH: CH₂Cl₂ (1:1; 3 x 5 minutes each), a solution of 8-hydroxyquinoline in CH₂Cl₂ (5% w/v; 5 x 1 hour and 1 x 12 hours each), CH₂Cl₂ (5 x 15 minutes each) and dried *in vacuo*.⁴⁰ In order to cleave the substrate from the polymer-support, the beads were suspended in a solution of HF-pyridine in THF (5% v/v) and shaken for 1.5 hours in a clear, washed Eppendorf® tube, then TMSOMe (to give a 1:1 v/v solution) was added and the mixture shaken for 30 minutes. The solution was filtered through a short pad of SiO₂ and concentrated *in vacuo*.

(P,10S)-5-{10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl}-pentan-1-ol; (P)-20aaa. Colorless oil; yield: 86%; kinetic dr: 7:1 (*P:M*); *R_f* 0.19 (SiO₂; Hexane: EtOAc; 7:3); ν_{max} (thin film)/cm⁻¹ 3333m, 2926s, 2856s, 1454s, 1366m, 1197m, 1093s, 757s, 699s; δ_H (500MHz, CDCl₃) 1.26-1.60 (6H, m, CH₂), 2.01 (1H, br s, OH), 2.29 (1H, dd, *J*13.5, 8Hz, PhCHH'), 2.35-2.43 (1H, m, NCHH'), 2.49-2.63 (3H, m, NCHH', C(3)H & PhCHH'), 3.11 (1H, dd, *J*12, 9.5Hz, C(2)H), 3.25 (1H, dd, *J*12, 3.5Hz, C(2)H), 3.63 (2H, t, *J*6.5Hz, CH₂OH), 3.66-3.79 (2H, ABq, *J*15Hz, C(5)H₂), 4.17 (1H, d, *J*12Hz, C(10)H), 4.40 (1H, d, *J*12Hz, C(10)H), 6.94 (1H, d, *J*7Hz, aryl CH), 7.08-7.41 (12H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.55, 27.68, 32.82, 38.05, 49.52, 53.60, 62.97, 64.75, 72.29, 73.55, 125.60, 126.11, 126.84, 127.14, 127.68, 127.91, 128.89, 129.47, 129.93, 130.18, 130.47, 137.73, 139.43, 139.89, 141.01, 142.74; *m/z* (ES) 416 (MH⁺, 100%); HRMS found 416.2603, C₂₈H₃₄NO₂ (MH⁺) requires 416.2589.

(M,10S)-5-{10-Benzyl-9-methyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl}-pentan-1-ol; (M)-20aaa. Colorless oil; thermodynamic dr: 1:7 (*P:M*); *R_f* 0.16 (SiO₂; Hexane: EtOAc; 7:3); ν_{max} (thin film)/cm⁻¹ 3385m, 2928s, 2858s, 1496s, 1455s, 1375s, 1085s, 755s, 698s; δ_H (500MHz, CDCl₃) 1.25-1.60 (7H, m, CH₂ & OH), 2.34 (1H, dd, *J*13.5, 6.5Hz, PhCHH'), 2.48-2.54 (1H, m, NCHH'), 2.61 (1H, dd, *J*13.5, 8Hz, PhCHH'), 2.77-2.83 (1H, m, NCHH'), 3.27 (1H, dd, *J*12.5, 4Hz, C(2)H), 3.67-3.42 (1H, m, C(3)H), 3.63 (2H, t, *J*7Hz, CH₂OH), 3.66 (1H, d, *J*12Hz, C(5)H), 3.82 (1H, dd, *J*12.5, 10.5Hz, C(2)H), 3.84 (1H, d, *J*12Hz, C(5)H), 4.15 (1H, d, *J*10Hz, C(10)H), 4.27 (1H, d, *J*10Hz, C(10)H), 7.00-7.42 (13H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.52, 27.85, 32.75, 36.29, 47.17, 53.08, 53.80, 62.95, 67.96, 69.05, 125.62, 126.25, 127.35, 127.55, 127.75, 128.02, 129.12, 129.69, 130.04, 130.15, 130.42, 134.87, 137.72, 139.87,

(38) To a solution of *i*-PrMgCl (1.0 equiv.) in 2-MeTHF (3 ml) at 0°C was added *n*-BuLi (2.0 equiv.) and the mixture stirred for 30 minutes to give a clear, pale yellow solution.

(39) The metallated, gel-phase substrate could be quenched at this stage by the addition of MeOH (0.5 ml). **(S)-5-[Benzyl-(1-benzoyloxymethyl-2-phenylethyl)-amino]-pentan-1-ol; 17aaa.** Colorless oil; yield: 97%; *R_f* 0.30 (SiO₂; Hexane: EtOAc; 2:1); ν_{max} (thin film)/cm⁻¹ 3383m br, 3084m, 3061m, 3026m, 2932s, 2858s, 1602m, 1495s, 1453s, 1362m, 1073s, 1028s, 736s, 698s; δ_H (500MHz, CDCl₃) 1.16-1.42 (6H, m, CH₂), 1.52 (1H, br s, OH), 2.51-2.63 (2H, m, NCH), 2.76-2.84 (2H, m, PhCH₂), 3.11-3.16 (1H, m, NCH), 3.46 (1H, dd, *J*10, 5Hz, CHH'OBn), 3.47 (2H, t, *J*6.5Hz, CH₂OH), 3.56 (1H, dd, *J*10, 6Hz, CHH'OBn), 3.72 (2H, s, NCH₂Ph), 4.39-4.45 (2H, ABq, *J*12Hz, OCH₂Ph), 7.12-7.33 (15H, m, aryl CH); δ_c (100MHz, CDCl₃) 23.45, 28.68, 32.87, 35.07, 50.48 & 55.35 (6 x CH₂), 61.03 (CH), 63.14, 70.72 & 73.35 (3 x CH₂), 126.03, 126.80, 127.76, 127.81, 128.30, 128.44, 128.61, 128.81 & 129.70 (9 x CH), 138.90, 140.98 & 141.46 (3 x quaternary); *m/z* (ES) 418 (MH⁺, 100%); HRMS found 418.2738, C₂₈H₃₆NO₂ (MH⁺) requires 418.2746. Found: C, 80.6; H, 8.60; N, 3.5%. C₂₈H₃₅NO₂ requires C, 80.5; H, 8.50; N, 3.4%.

(40) In order to obtain the thermodynamically more stable diastereomer, the beads were heated under argon at 120-150°C for 24-48 hours before cleaving the substrate off the polymer-support with HF-pyridine.

(37) The cyclization precursor was dried by being azeotroped twice with benzene, then dried at 50°C *in vacuo* for 1 hour.

140.87, 141.94; m/z (ES) 416 (MH^+ , 100%); HRMS found 416.2605, $C_{28}H_{34}NO_2$ (MH^+) requires 416.2589.

(M,10R)-5-{17-Fluoro-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl}-pentan-1-ol; (M)-20fab. Colorless oil; yield: 72%; kinetic dr: 1:5 ($P:M$); R_f 0.34 (SiO_2 ; Hexane: EtOAc; 7:3); ν_{max} (thin film)/ cm^{-1} 3391m br, 2929s, 2862s, 1585s, 1481s, 1451s, 1177m, 1103s, 898m, 826m, 765s, 702s; δ_H (500MHz, $CDCl_3$) 1.13-1.48 (6H, m, CH_2), 1.58 (1H, br s, OH), 2.33-2.47 (2H, m, NCH_2), 3.10 (1H, t, J 10Hz, C(2)H), 3.48 (1H, d, J 15.5Hz, C(5)H), 3.52 (2H, t, J 6.5Hz, CH_2OH), 3.53 (1H, dd, J 10, 2Hz, C(2)H or C(3)H), 3.69 (1H, dd, J 10, 2Hz, C(2)H or C(3)H), 3.70 (1H, d, J 10Hz, C(10)H), 4.20 (1H, d, J 15.5Hz, C(5)H), 4.44 (1H, d, J 10Hz, C(10)H), 6.97-7.36 (10H, m, aryl CH), 7.52 (1H, td, J 7.5, 1Hz, aryl CH), 8.07 (1H, d, J 8Hz, aryl CH); δ_C (100MHz, $CDCl_3$) 23.49, 27.13, 32.71, 51.37, 55.94, 63.10, 68.92, 72.55, 76.67, 114.12 (d, J 20.5Hz), 117.32 (d, J 21Hz), 125.96, 127.33, 127.98, 128.31, 128.53, 129.58, 130.36, 130.70 (d, J 9Hz), 133.28, 138.43, 142.46, 143.17, 145.13 (d, J 8Hz), 162.57 (d, J 247.5Hz); m/z (ES) 420 (MH^+ , 100%); HRMS found 420.2322, $C_{27}H_{31}FNO_2$ (MH^+) requires 420.2339. Found: C, 77.2; H, 7.10; N, 3.2%. $C_{27}H_{30}FNO_2$ requires C, 77.3; H, 7.20; N, 3.3%.

(P,10R)-5-{17-Fluoro-10-phenyl-12-oxa-9-azatricyclo[12.4.0.0^{2,7}]octadeca-1(14),2,4,6,15,17-hexaen-9-yl}-pentan-1-ol; (P)-20fab. Colorless oil; thermodynamic dr: 2:1 ($P:M$); R_f 0.26 (SiO_2 ; Hexane: EtOAc; 1:1); ν_{max} (thin film)/ cm^{-1} 3415m br, 3058m, 2932s, 2859s, 1612m, 1584s, 1482s, 1224s, 1177s, 1079s, 753s, 697s; δ_H (500MHz, $CDCl_3$) 1.12-1.45 (6H, m, CH_2), 1.60 (1H, br s, OH), 2.43-2.52 (2H, m, NCH_2), 3.49 (2H, t, J 6.5Hz, CH_2OH), 3.79-3.82 (1H, m, C(2)H or C(3)H), 3.83 (1H, d, J 12Hz, C(5)H), 4.00 (1H, d, J 12Hz, C(5)H), 4.22-4.27 (2H, m, remaining C(2)H and C(3)H), 4.28-4.37 (2H, ABq, J 10Hz, C(10)H), 6.91 (1H, dd, J 9.5, 3Hz, aryl CH), 7.08-7.48 (10H, m, aryl CH), 7.82 (1H, d, aryl CH); δ_C (100MHz, $CDCl_3$) 23.03, 27.50, 32.54, 47.24, 52.75, 53.69, 63.20, 67.06, 67.35, 114.91 (d, J 21Hz), 117.70 (d, J 21.5Hz), 126.91, 127.09, 128.13, 128.21, 128.54, 130.14, 130.55, 131.42 (d, J 3Hz), 132.39 (d, J 9Hz), 138.61, 140.59, 141.29, 144.55 (d, J 8Hz), 162.52 (d, J 248Hz); m/z (ES) 420 (MH^+ , 100%); HRMS found 420.2350, $C_{27}H_{31}FNO_2$ (MH^+) requires 420.2339. Found: C, 77.1; H, 7.10; F, 4.4; N, 3.3%. $C_{27}H_{30}FNO_2$ requires C, 77.3; H, 7.20; F, 4.5; N, 3.3%.

(M,10R)-5-{10-Phenyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-1(14),2,4,6,15,17(22),18,20-octaen-9-yl}-pentan-1-ol; (M)-20fac. Colorless oil; yield: 87%; kinetic dr: 1:1.5 ($P:M$); R_f 0.30 (SiO_2 ; Hexane: EtOAc; 7:3); ν_{max} (thin film)/ cm^{-1} 3375m br, 2929s, 1599s, 1451s, 1382s, 1103s, 820m, 752s, 701s; δ_H (500MHz, $CDCl_3$) 1.09-1.43 (6H, m, CH_2), 1.57 (1H, br s, OH), 2.05-2.29 (1H, m, NCH_2), 2.35-2.41 (1H, m, NCH_2), 3.18 (1H, dd, J 10.5, 9.5Hz, C(2)H), 3.43 (1H, d, J 15.5Hz, C(5)H), 3.49 (2H, t, J 6.5Hz, CH_2OH), 3.59 (1H, dd, J 10.5, 2Hz, C(2)H or C(3)H), 3.64 (1H, dd, J 9.5, 2Hz, C(2)H or C(3)H), 3.96 (1H, d, J 10.5Hz, C(10)H), 4.05 (1H, d, J 15.5Hz, C(5)H), 4.61 (1H, d, J 10.5Hz, C(10)H), 7.08 (1H, dd, J 7.5, 1.5Hz, aryl CH), 7.21-7.49 (9H, m, aryl CH), 7.52 (1H, d, J 8.5Hz, aryl CH), 7.58 (1H, td, J 7.5, 1Hz, aryl CH), 7.90 (1H, d, J 8.5Hz, aryl CH), 7.91 (1H, d, J 8Hz, aryl CH), 8.13 (1H, d, J 8Hz, aryl CH); δ_C (100MHz, $CDCl_3$) 23.21, 26.87, 32.47, 51.06, 55.36 & 62.88 (6 x CH_2), 68.68 (CH), 73.65 & 76.71 (2 x CH_2), 125.74, 125.81, 125.99, 126.85, 127.00, 127.16, 127.67, 127.79, 127.84, 127.99, 128.25, 130.24 & 130.30 (13 x CH), 133.32, 133.38, 134.09, 136.94, 139.42, 143.00 & 143.16 (7 x quaternary); m/z (ES) 452 (MH^+ , 100%); HRMS found 452.2586, $C_{31}H_{34}NO_2$ (MH^+) requires 452.2589.

(P,10R)-5-{10-Phenyl-12-oxa-9-azatetracyclo[12.8.0.0^{2,7}.0^{13,22}]docosa-1(14),2,4,6,15,17(22),18,20-octaen-9-yl}-pentan-1-ol; (P)-20fac. Colorless oil; R_f 0.27 (SiO_2 ; Hexane: EtOAc; 7:3); ν_{max} (thin film)/ cm^{-1} 3417m br, 2934s, 1599m, 1450s, 1382s, 1063s, 821s, 751s, 699s; δ_H (500MHz, $CDCl_3$) 1.06-1.40 (6H, m, CH_2), 1.56 (1H, br s, OH), 2.11-2.16 (1H, m, NCH_2), 2.33-2.39 (1H, m, NCH_2), 3.47 (1H, d, J 12Hz, C(5)H), 3.48 (2H, t, J 6.5Hz, CH_2OH), 3.78 (1H, d, J 12Hz, C(5)H), 3.80 (1H, dd, J 12.5, 6.5Hz, C(2)H), 3.94 (1H, dd, J 12.5, 6Hz, C(2)H or C(3)H), 4.13 (1H, t, J 7Hz, C(2)H or C(3)H), 4.50 (1H, d, J 11Hz, C(10)H), 4.59 (1H, d, J 11Hz, C(10)H), 7.11 (1H, dd, J 7.5, 1.5Hz, aryl CH), 7.19-7.53 (10H, m, aryl CH), 7.65 (1H, d, J 8Hz, aryl CH), 7.85 (1H, dd, J 8, 1Hz, aryl CH), 7.91 (1H, d, J 8Hz, aryl CH), 7.94 (1H, d, J 8Hz, aryl CH); δ_C (100MHz, $CDCl_3$) 23.02, 27.58, 32.59, 47.90, 52.15, 53.94, 63.15, 64.20, 67.48, 126.26, 126.42, 126.73, 127.12, 127.98, 128.02, 128.18, 128.19, 128.54, 130.64, 131.37, 132.73, 133.51, 133.58, 139.15, 139.23, 139.70, 141.90; m/z (ES) 452 (MH^+ , 100%); HRMS found 452.2591, $C_{31}H_{34}NO_2$ (MH^+) requires 452.2589.

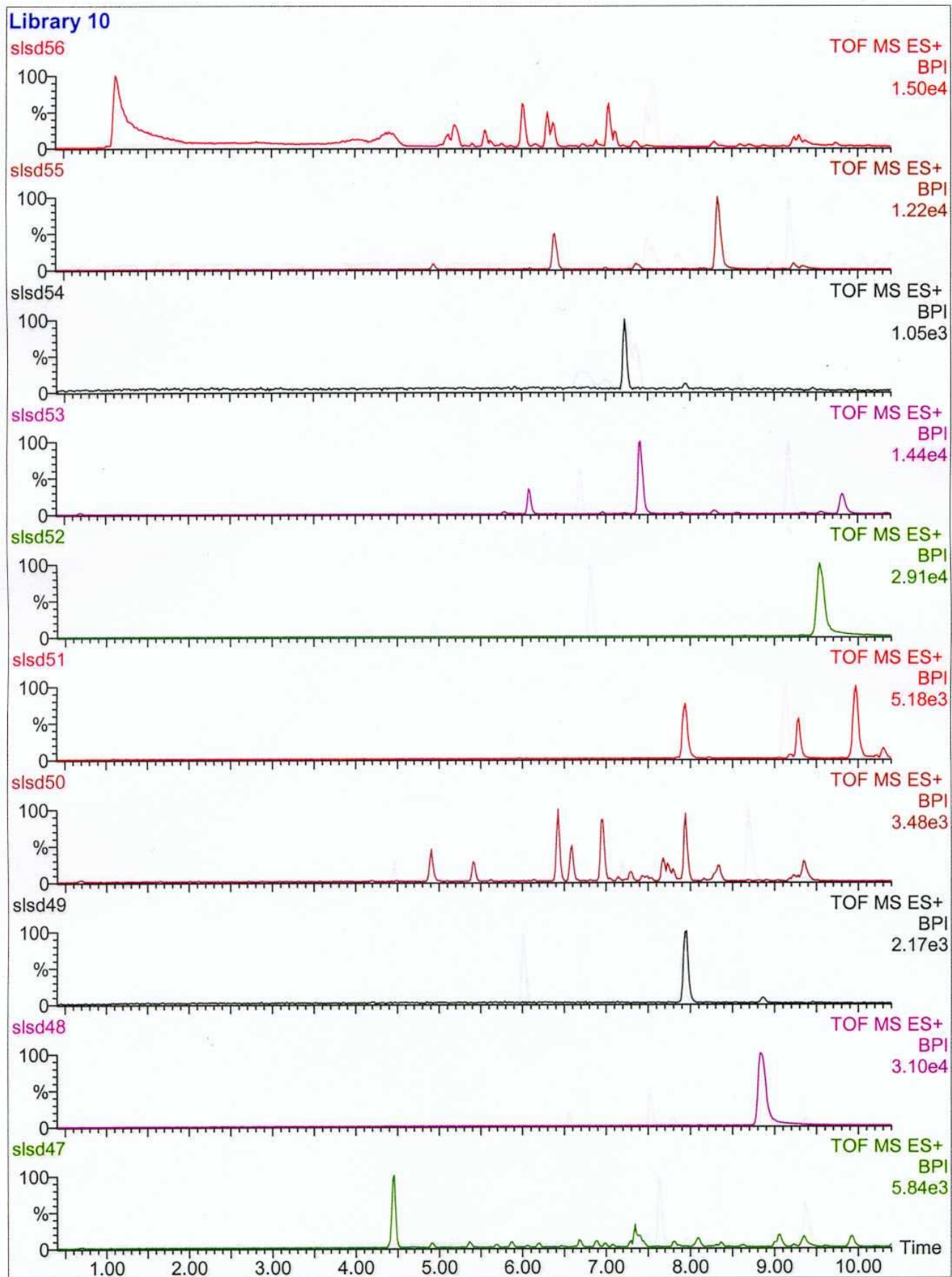
(M,10R)-5-{4,5-Dimethoxy-10-phenyl-12,17,19-trioxa-9-azatetracyclo[12.7.0.0^{2,7}.0^{16,20}]uncosa-1(14),2,4,6,15,20-hexaen-9-yl}-pentan-1-ol; (M)-20fdd. White crystals; yield: 74%; kinetic dr: 1:8 ($P:M$); m.p. 172-173°C (*i*-PrOH); R_f 0.28 (SiO_2 ; Hexane: EtOAc; 1:1); ν_{max} (KBr disc)/ cm^{-1} 3427m br, 2932s, 1603w, 1514m, 1502m, 1483s, 1244s, 1207m, 1131m, 1103s, 1039s, 933m, 871m, 731m, 702m; δ_H (500MHz, $CDCl_3$) 1.28-1.49 (6H, m, CH_2), 1.55 (1H, br s, OH), 2.34-2.48 (2H, m, NCH_2), 3.14 (1H, t, J 10Hz, C(2)H), 3.41 (1H, d, J 15Hz, C(5)H), 3.48 (2H, t, J 6Hz, CH_2OH), 3.52 (1H, dd, J 10, 1.5Hz, C(2)H or C(3)H), 3.67 (1H, d, J 10.5Hz, C(10)H), 3.69 (1H, dd, J 10, 1.5Hz, C(2)H or C(3)H), 3.84 (3H, s, OCH_3), 4.05 (3H, s, OCH_3), 4.20 (1H, d, J 15Hz, C(5)H), 4.35 (1H, d, J 10.5Hz, C(10)H), 5.99 (2H, apparent d, J 6Hz, OCH_2O), 6.54 (1H, s, aryl CH), 6.75 (1H, s, aryl CH), 6.83 (1H, s, aryl CH), 7.21-7.37 (5H, m, aryl CH), 7.62 (1H, s, aryl CH); δ_C (100MHz, $CDCl_3$) 23.59, 27.06, 32.71, 51.09, 55.86, 56.07, 56.16, 62.94, 68.81, 73.31, 76.72, 101.45, 109.72, 110.95, 112.69, 112.73, 127.33, 127.92, 128.52, 131.03, 135.27, 136.24, 143.43, 146.80, 147.37, 148.65; m/z (ES) 506 (MH^+ , 100%); HRMS found 506.2555, $C_{30}H_{36}NO_6$ (MH^+) requires 506.2542. Found: C, 71.1; H, 6.90; N, 2.7%. $C_{30}H_{35}NO_6$ requires C, 71.3; H, 7.00; N, 2.8%.

(P,10R)-5-{4,5-Dimethoxy-10-phenyl-12,17,19-trioxa-9-azatetracyclo[12.7.0.0^{2,7}.0^{16,20}]uncosa-1(14),2,4,6,15,20-hexaen-9-yl}-pentan-1-ol; (P)-20fdd. Colorless oil; thermodynamic dr: 2:1 ($P:M$); R_f 0.27 (SiO_2 ; Hexane: EtOAc; 1:1); ν_{max} (thin film)/ cm^{-1} 3441m br, 2934s, 1604m, 1516s, 1502s, 1484s, 1226s, 1139s, 1081s, 1039s, 731s, 699s; δ_H (500MHz, $CDCl_3$) 1.23-1.48 (6H, m, CH_2), 2.41-2.55 (2H, m, NCH_2), 3.50 (2H, t, J 6.5Hz, CH_2OH), 3.79 (1H, d, J 11.5Hz, C(5)H), 3.79-3.83 (1H, m, C(2)H or C(3)H), 3.84 (3H, s, OCH_3), 3.91 (1H, d, J 11.5Hz, C(5)H), 3.98 (3H, s, OCH_3), 4.18-4.24 (2H, m, remaining C(2)H and C(3)H), 4.25-4.30 (2H, ABq, J 10.5Hz, C(10)H), 6.02 (2H, apparent dd, J 10.5, 0.5Hz, OCH_2O), 6.59 (1H, s, aryl CH), 6.68 (1H, s, aryl CH), 6.96 (1H, s, aryl CH), 7.19-7.37 (6H, m, aryl CH); δ_C (100MHz, $CDCl_3$) 23.20, 27.74, 32.56, 47.49, 52.67, 53.17, 56.11, 56.13, 63.18, 66.32, 67.74, 101.53, 110.37, 110.99, 111.95, 113.28, 126.80, 127.91, 128.19, 129.10, 130.99, 133.58, 135.98, 141.76, 147.37, 147.62, 147.71, 148.98; m/z (ES) 506 (MH^+ , 100%); HRMS found 506.2547, $C_{30}H_{36}NO_6$ (MH^+) requires 506.2542. Found: C, 71.0; H, 6.80; N, 2.7%. $C_{30}H_{35}NO_6$ requires C, 71.3; H, 7.00; N, 2.8%.

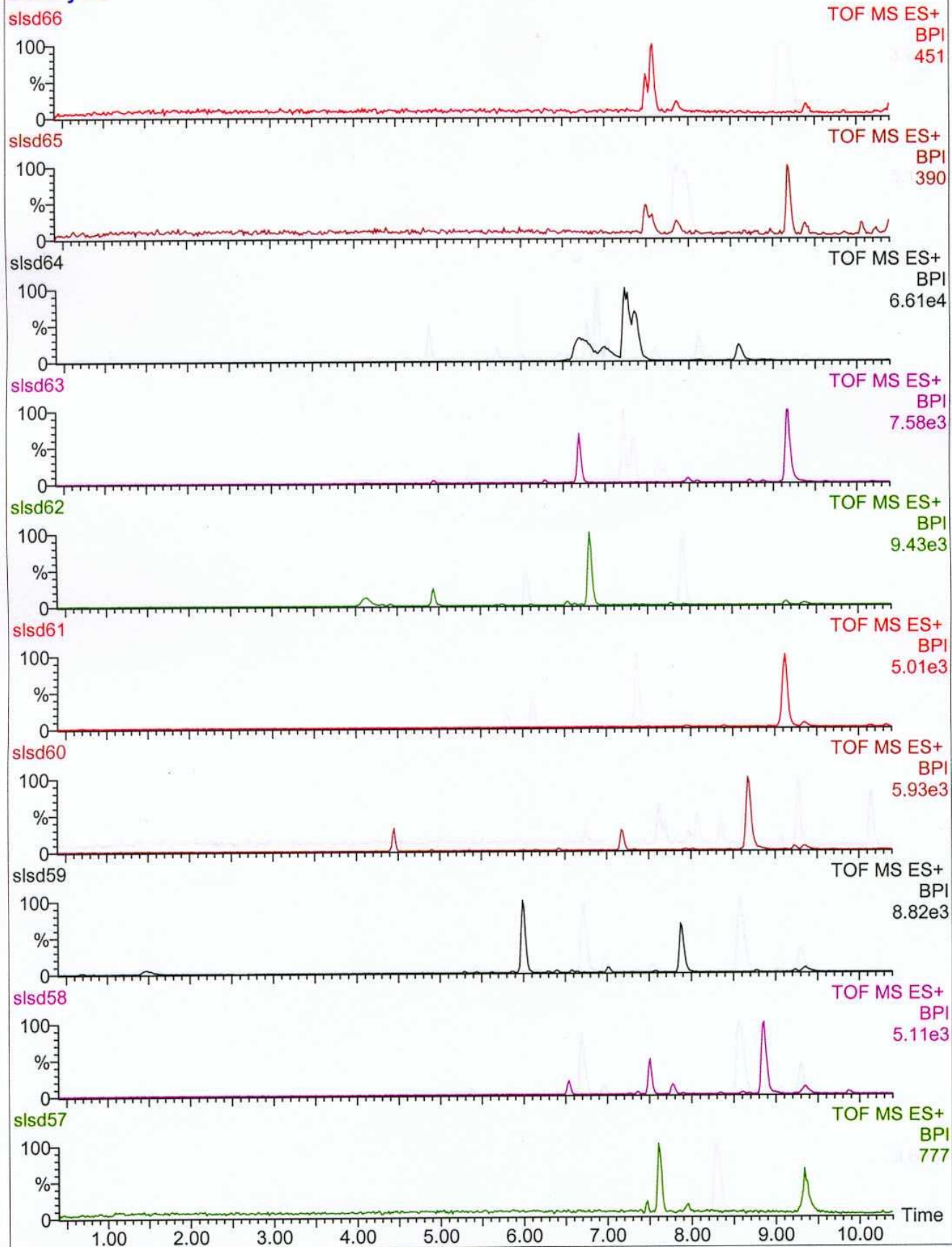
(10R)-5-{10-phenyl-8-oxa-4-thia-11-azatricyclo[11.4.0.0^{2,7}]heptadeca-1(13),2,5,14,16-pentaen-9-yl}-pentan-1-ol; 20fae. Colorless oil; yield: 74%; R_f 0.21 (SiO₂; Hexane: EtOAc; 7:3); ν_{max} (thin film)/cm⁻¹ 3389m br, 2933s, 2860s, 1599m, 1492s, 1450s, 1366s, 1079s, 863m, 801m, 766s, 698s; δ_H (500MHz, CDCl₃; CF₃CO₂H, 100:1)⁴¹ 1.33-1.43 (2H, m, NCH₂CH₂CH₂), 1.68-1.76 (3H, m, CH₂CH₂OH and NCH₂CH), 1.95-2.05 (1H, br m, NCH₂CH), 3.28 (1H, br td, J_{12} , 5Hz, NCH), 3.54 (1H, br t, J_{12} Hz, NCH), 3.73 (1H, dd, J_{14} , 4Hz, C(2)H), 4.07 (1H, d, $J_{10.5}$ Hz, C(5)H or C(10)H), 4.28 (2H, apparent octet, $J_{5.5}$ Hz, CH₂OH), 4.48 (1H, d, J_{13} Hz, C(5)H or C(10)H), 4.64 (1H, t, J_{14} Hz, C(2)H), 4.68 (1H, d, $J_{10.5}$ Hz, C(5)H or C(10)H), 4.73 (1H, d, J_{13} Hz, C(5)H or C(10)H), 4.98 (1H, br dd, J_{14} , 4Hz, C(3)H), 7.21-7.54 (9H, m, aryl CH), 7.73 (1H, t, $J_{7.5}$ Hz, aryl CH), 8.33 (1H, d, $J_{7.5}$ Hz, aryl CH); δ_C (100MHz, CDCl₃; CF₃CO₂H, 100:1) 23.16, 24.09, 27.59, 49.95 & 56.02 (5 x CH₂), 58.86 (CH), 65.21, 65.85 & 67.56 (3 x CH₂), 126.50, 127.30 & 128.89 (3 x CH), 129.06 (quaternary), 129.50, 129.80 & 129.86 (3 x CH), 129.91 (quaternary), 130.26, 131.08 & 132.80 (3 x CH), 135.28, 137.35 & 140.60 (3 x quaternary); m/z (ES) 408 (MH⁺, 100%); HRMS found 408.1981, C₂₅H₃₀NO₂S (MH⁺) requires 408.1997.

(10R)-5-{4,5-Dimethoxy-10-phenyl-17-chloro-12-oxa-21-thia-9-azatetracyclo[12.7.0.0^{2,7}.0^{15,20}]uncosa-1(14),2,4,6,15,17,19-heptaen-9-yl}-pentan-1-ol; 20fdf. Colorless oil; yield: 90%; R_f 0.31 (SiO₂; Hexane: EtOAc; 1:1); ν_{max} (thin film)/cm⁻¹ 3432m br, 2933s, 2859s, 1603m, 1510s, 1462s, 1440s, 1382m, 1244s, 1208m, 1136s, 1077s, 1041m, 868m, 802m, 744m, 700s; δ_H (500MHz, CDCl₃, 50°C) 1.16-1.51 (6H, m, CH₂), 2.39-2.51 (2H, m, NCH₂), 3.51 (2H, t, $J_{6.5}$ Hz, CH₂OH), 3.55 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.80 (1H, dd, $J_{12.5}$, 5.5Hz, C(2)H), 3.86 (3H, s, OCH₃), 3.95 (1H, d, $J_{12.5}$ Hz, C(5)H), 3.97 (3H, s, OCH₃), 4.07-4.13 (1H, m, C(2)H or C(3)H), 4.30 (1H, br t, $J_{6.5}$ Hz, C(2)H or C(3)H), 4.72-4.79 (2H, m, C(10)H₂), 6.83 (1H, s, aryl CH), 7.16 (1H, s, aryl CH), 7.21-7.36 (6H, m, aryl CH), 7.75 (1H, d, $J_{8.5}$ Hz, aryl CH), 7.95 (1H, d, J_{2} Hz, aryl CH); δ_C (100MHz, CDCl₃) 23.26, 27.80, 32.56, 48.07, 51.88, 55.23, 56.23, 56.26, 61.32, 63.08, 64.63, 113.17, 113.86, 122.47, 123.25, 125.36, 125.60, 127.04, 128.04, 128.27, 129.42, 131.40, 132.27, 137.72, 140.50, 140.87, 145.23, 147.89, 150.08; m/z (ES) 552 (MH⁺, ³⁵Cl, 100%), 554 (MH⁺, ³⁷Cl, 45%); HRMS found 552.1973, C₃₁H₃₅ClNO₄S (MH⁺, ³⁵Cl) requires 552.1978.

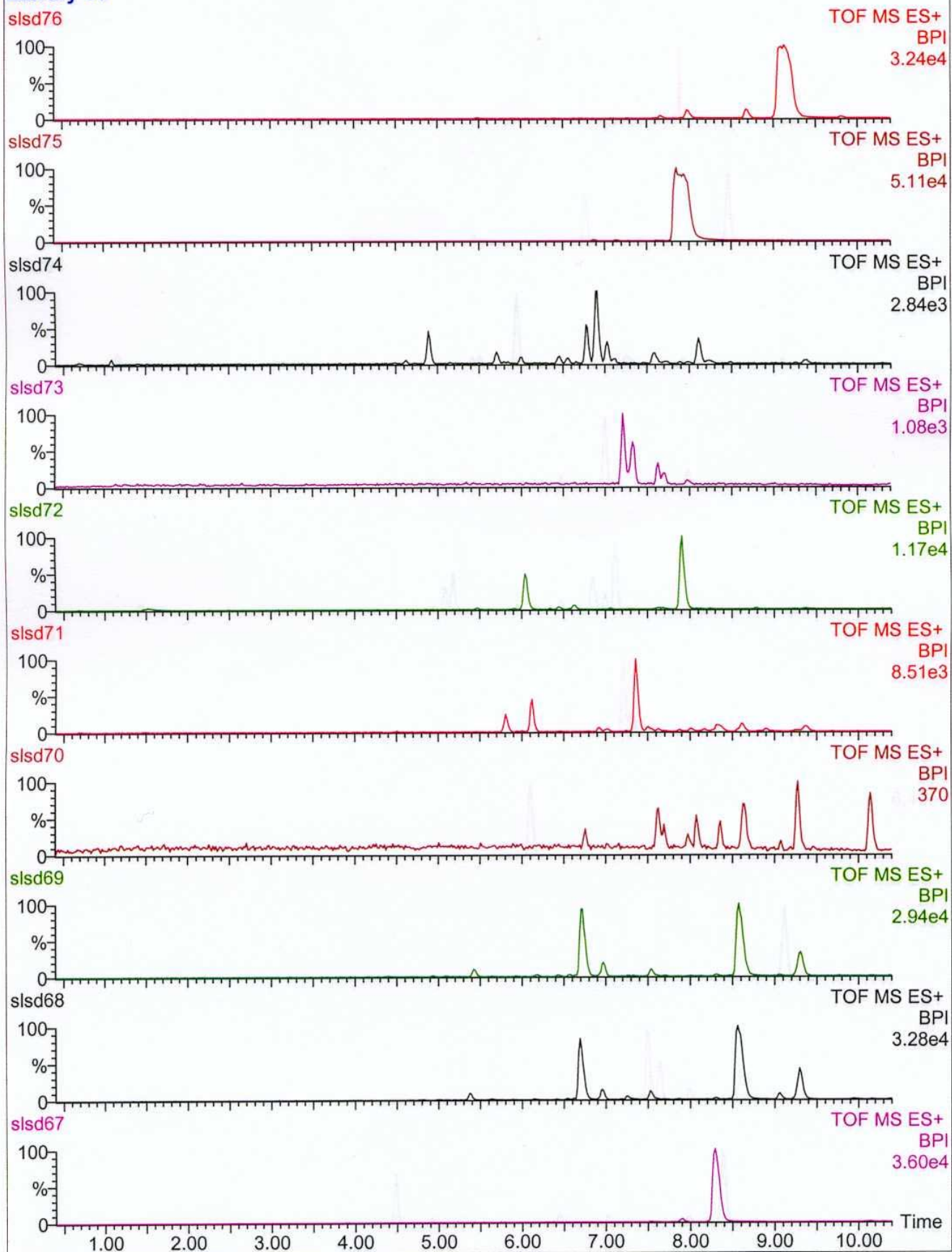
(41) A mixture of rotomers was observed in CDCl₃ (3:1), C₆D₆ (5:2) and C₆D₅CD₃ (5:2 at 22°C; 2:1 at 100°C), even at elevated temperatures. Protonation of the tertiary amine with trifluoroacetic acid simplifies the proton NMR spectrum into a single set of proton signals, presumably by influencing the dynamic equilibrium between ring conformations.



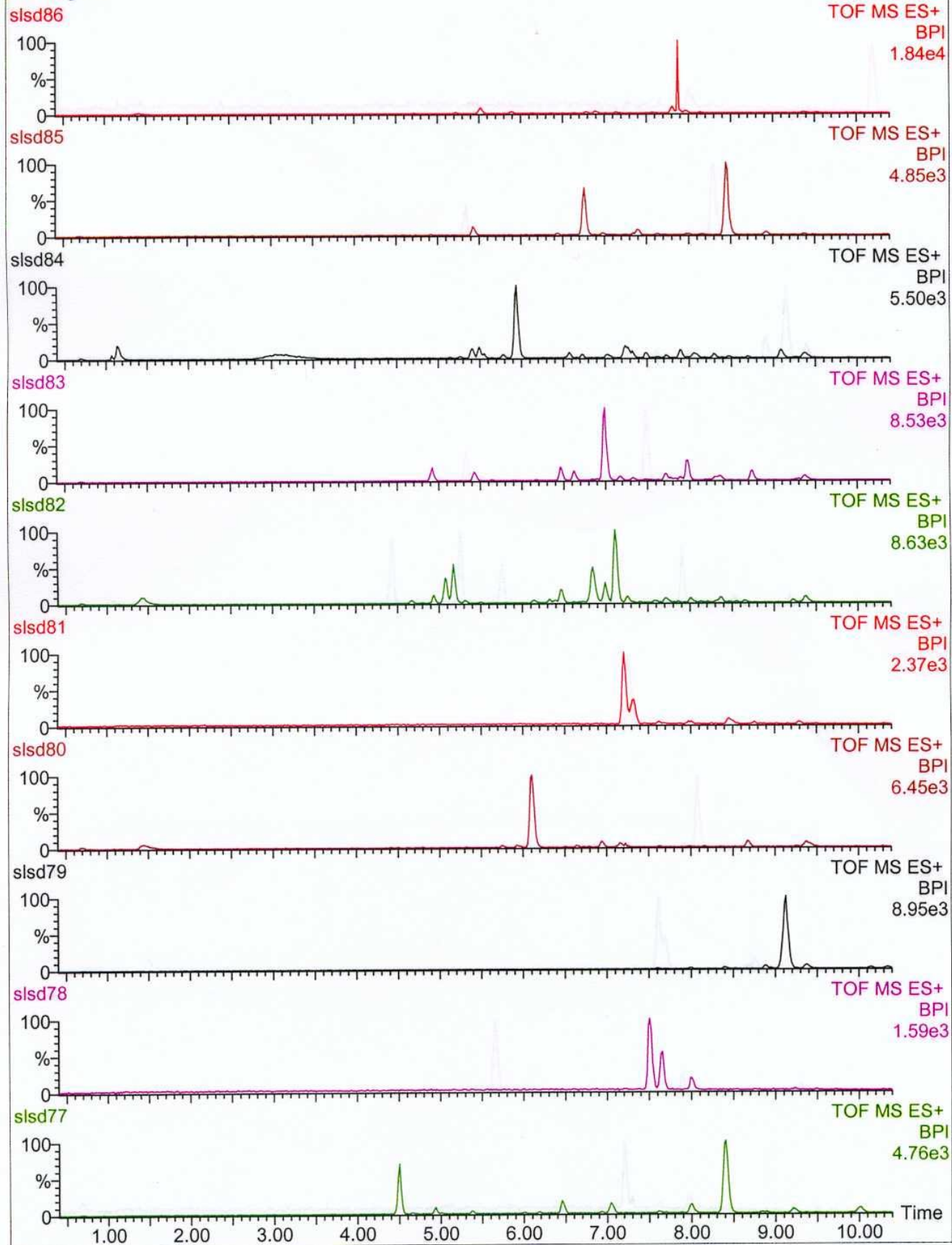
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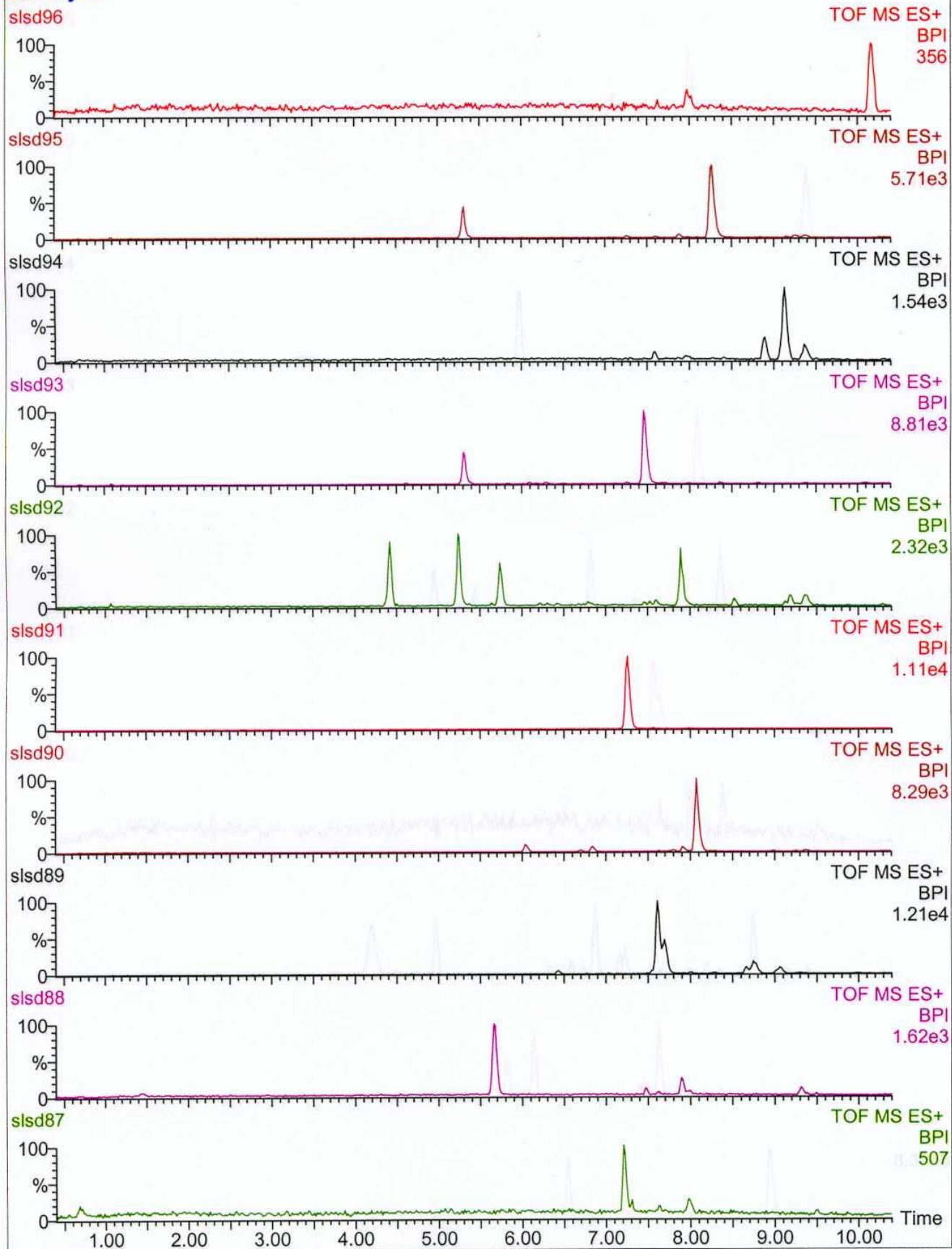
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Library 40

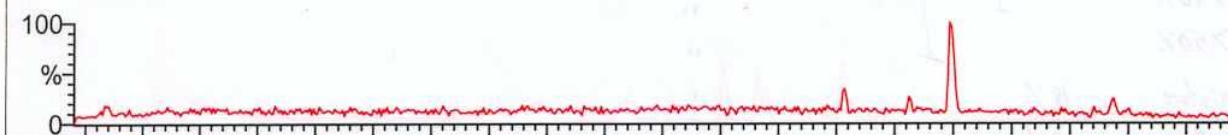


Library 50



Library 60

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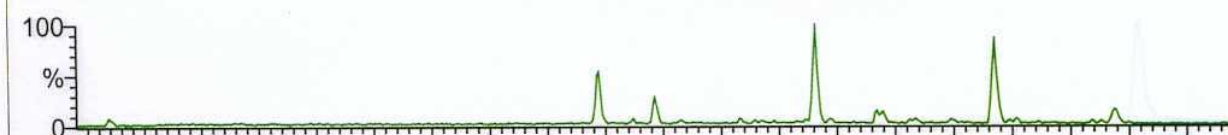
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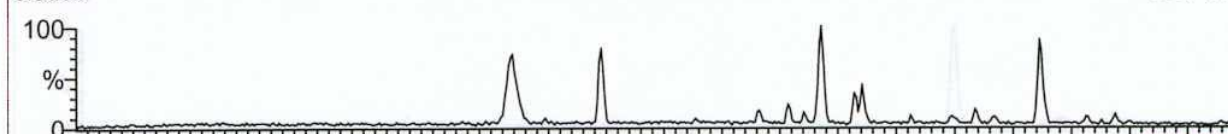
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Time